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促进学术交流，引领生殖学科 健康发展

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伴随着新年的钟声，我们送别了满载收获的 2018 年，带着激情和梦想迎来了 2019。值此辞旧迎新之际，《中华生殖与避孕杂志》向长期以来指导、支持和关心本刊发展的各级领导、各位编委、广大读者及企业界的朋友致以衷心的感谢和崇高的敬意，祝愿大家在新的 一年里事业发达、身体健康、阖家幸福！

《中华生殖与避孕杂志》在各位领导、编委和编辑的共同努力下，取得了一系列成绩，期刊质量不断攀升。本杂志被收录于《中文核心期刊要目总览》2017 年版、中国科学引文数据库，是中国科技核心期刊、《中国学术期刊影响因子年报》统计源期刊。2018 年本杂志的复合影响因子（中国知网发布）上升为 1.479，并荣获“中国精品科技期刊”称号，编辑部也获得“上海市巾帼文明岗”荣誉称号。编辑部全体同仁精益求精，严把稿件质量关，不断进行改革与创新。2017—2018 年，编辑部紧跟研究发展动态，共刊出专题刊或专题栏 7 个，述评 7 篇，组织专家讨论并撰写“高龄女性不孕诊治指南”、“低分子肝素防治自然流产中国专家共识”和“基于单次促排卵周期的累积分娩 / 活产率专家共识”，为疾病的临床诊治流程和用药注意事项提供参考。2018 年 3 月，编辑部成功举办期刊专场论坛，邀请编委专家现场讲解实验设计、数据分析、实验动物模型的正确选用、述评和综述的写作要点及中英文论文写作、投稿的注意事项等，宣传期刊的同时积极培育我们的作者，促进学术交流。

当前，生育力下降已成为影响人类健康和可持续发展的三大疾病之一。现在中国总和生育率低于世界总和生育率，不孕率在 6%~18% 之间，即约有 2000 万对不孕不育夫妇。自我国全面“二孩”政策实施以来，前来寻求辅助生殖治疗的女性人数不断增加，且趋高龄化。高龄与多种因素叠加使卵母细胞活力降低，辅助生殖成功率下降，不易怀孕、怀上保不住以及出生缺陷发生率升高等不孕不育患者面临的问题逐渐增多。针对上述问题，2019 年本刊将继续关注生殖医学学科动态，聚焦学科热点：生育力保护、高危孕产、男性不育、家庭生育计划等，联系专家就反复种植失败、更年期诊疗规范、辅助生殖护理等问题出版共识及国外相关共识解读，以期规范临床诊疗。同时，我们将在原有栏目的基础上，开辟院士论坛等新栏目，针对目前生殖医学的热点和难点如大数据时代下的机器人与辅助生殖治疗、计划生育新认识、非肥胖型多囊卵巢综合征治疗、生育力保存等，邀请生殖领域的院士、专家进行高屋建瓴的梳理、讨论，以提升学科内涵，促进生殖学科健康发展。

为者常成，行者常至。在新的一年里，我们仍将全力以赴，做出更好的成绩，使更多创新性好、科学性强、学术价值高的优秀科研成果在本刊发表，助力于我国生殖医学领域的不断创新与发展。



总编：乔杰

人类精子核内胞质残留对受精后生殖活动的可能负效应

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【摘要】 人类精子核内含有残留胞质 (INCR)。INCR 起源于精子细胞变态过程的早期, 是核内含有胞质的一种隐匿性核异常类型。INCR 是人类精子核内多见的超微现象, 存在于精子核空泡内, 具有大小、形状、数量、成分、位置和分布的多样性。畸形精子症的精子标本中, INCR 发生率与精子头畸形率呈正相关。INCR 可能通过多重机制对受精后的父本基因组活动和合子、早期胚胎发育产生负效应。应重视 INCR 可能对受精后生殖活动的影响, 围绕 INCR 开展相关的实验与临床研究。

【关键词】 人类精子; 胞质残留; 细胞核; 超微结构; 精子变态

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Possible negative effects of human sperm intranuclear cytoplasmic retention on post-fertilization events

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【Abstract】 The human sperm nucleus contains intranuclear cytoplasmic retention (INCR). INCR occurs in the early process of spermatogenesis and is a hidden sperm nuclear alteration. Transmission electron microscopy revealed that INCR is a common ultrastructural phenomena within sperm nuclei. INCR existed in a nuclear vacuole and varied in size, number, shape, content, location, and distribution. In the teratozoospermia samples, the incidence of INCR exhibited a positive relationship with sperm abnormal morphology. INCR could play multiple harmful roles and contribute to deleterious impacts on post-fertilization events through different mechanisms. More experimental studies are needed to further elucidate INCR for basic and clinical aspects.

【Key words】 Human sperm; Cytoplasmic retention; Nucleus; Ultrastructure; Spermiogenesis

Fund program: Science and Technology Planning Project of Guangdong Province, China (2014A020213007)

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获单卵周期行体外受精 / 卵胞质内单精子显微注射的结局比较

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【摘要】目的 探讨不孕患者获 1 枚卵周期合理的授精方式的选择。**方法** 对 2014 年 1 月—2015 年 12 月期间在大连市妇女儿童医疗中心、山西省儿童医院山西省妇幼保健院生殖医学中心、沈阳东方菁华医院、沈阳市妇婴医院、中国医科大学附属盛京医院、天津市中心妇产科医院和河北医科大学第二医院生殖医学科因女方因素不孕行助孕治疗且获卵数为 1 枚的 965 例不孕症患者共计 965 个治疗周期临床资料进行回顾性队列分析。根据不同授精方式分为体外受精 (IVF) 组 (675 个周期) 和卵胞质内单精子显微注射 (ICSI) 组 (290 个周期)。比较 IVF 组和 ICSI 组患者的一般资料、受精率、胚胎发育情况和临床妊娠结局。**结果** IVF 组多原核 (PN) 率 (7.11%)、多 PN 总比率 (7.11%) 均明显高于 ICSI 组 (1.48%, 1.38%), 差异具有统计学意义 ($P < 0.01$)。IVF 组移植周期率 (34.22%) 明显高于 ICSI 组 (24.48%), 差异具有统计学意义 ($P < 0.01$)。IVF 组可移植周期率和可利用胚胎率略高于 ICSI 组, 但差异无统计学意义 ($P > 0.05$)。临床妊娠率、周期妊娠率和胚胎种植率组间比较差异均无统计学意义 ($P > 0.05$); IVF 组流产率 (15.38%) 略低于 ICSI 组 (41.67%) ($P = 0.05$)。**结论** 在仅有 1 枚卵细胞的治疗周期中, ICSI 授精并不能提高临床妊娠率、改善妊娠结局, IVF 授精是一种安全有效、又降低治疗成本的方式, 值得临床推广应用。

【关键词】 受精, 体外; 精子注射, 细胞质内; 生殖技术, 辅助; 1 枚获卵周期; 低获卵周期

DOI: 10.3760/cma.j.issn.2096-2916.2019.01.003 **【Key words】** Fertilization *in vitro*; Sperm injections, intracytoplasmic; Reproductive techniques, assisted; One egg cycle; Low egg acquisition cycle

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· 临床研究 ·

Study on application effect of *in vitro* fertilization/intracytoplasmic sperm injection in one egg cycle

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【Abstract】 Objective To provide a clinical basis for selecting a reasonable fertilization method for infertile patients with one egg in the future. **Methods** A retrospective cohort study was conducted in Dalian Municipal Women and Children's Medical Center, Center of Reproductive Medicine, Children's Hospital of Shanxi and Women Health Center of Shanxi, Shenyang Dongfang Jinghua Hospital, Shenyang Women's and Children's Hospital, Shengjing Hospital of China Medical University, Tianjin Central Hospital of Gynaecology and Obstetrics and the Second Hospital of Hebei Medical University from January 2014 to December 2015. A total of 965 infertility patients who were assisted by fertility medicine and got one egg were divided into *in vitro* fertilization (IVF) group ($n=675$) and intracytoplasmic sperm injection (ICSI) group ($n=290$) according to different insemination methods. The general data, fertilization rate, embryonic development and clinical pregnancy outcomes were compared between the two groups. **Results** The multiple pronucleus (PN) rate and multiple PN rate of all eggs in IVF group (7.11%, 7.11%) were significantly higher than those in ICSI group (1.48%, 1.38%) ($P<0.01$). The rate of embryo transfer cycle in IVF group (34.22%) was significantly higher than that in ICSI group (24.48%) ($P<0.01$). The IVF group had higher rates of transplantable cycles and available embryos than ICSI group, but there was no significant difference. There was no significant difference in clinical pregnancy rate, cycle pregnancy rate and embryo implantation rate between the two groups ($P>0.05$). The IVF group (15.38%) had a slightly lower miscarriage rate than ICSI group (41.67%), but the difference was not statistically significant ($P=0.05$). **Conclusion** ICSI insemination can not improve clinical pregnancy rate or pregnancy outcomes during the treatment cycle of only one egg. Therefore, IVF insemination is a safe and effective way to reduce the cost of treatment, which is worthy of clinical application

【Key words】 Fertilization *in vitro*; Sperm injections, intracytoplasmic; Reproductive techniques, assisted; One egg cycle; Low egg acquisition cycle

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未孕的复发性流产患者抗甲状腺抗体与外周血淋巴细胞亚群之间关系的研究

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【摘要】目的 探讨抗甲状腺抗体 (ATA) 阳性的复发性流产 (RSA) 患者未孕时的细胞免疫状态, 及其发病机制。**方法** 选择 2015 年 12 月—2016 年 12 月期间就诊于盛京医院门诊的未孕 RSA 患者 200 例进行回顾性病例对照研究, 根据 ATA 水平及甲状腺功能状态将其分组: ATA 阳性 86 例, 记为 ATA⁺ 组, 其中促甲状腺激素 (TSH) ≥ 2.50 mIU/L 36 例, 记为 ATA⁺ high 组, TSH < 2.50 mIU/L 50 例, 记为 ATA⁺ normal 组; ATA 阴性 114 例, 记为 ATA⁻ 组, 其中 TSH ≥ 2.50 mIU/L 50 例, 记为 ATA⁻ high 组, TSH < 2.50 mIU/L 64 例, 记为 ATA⁻ normal 组。比较各组之间各淋巴细胞亚群的差异。**结果** ① ATA⁺ high 组 CD16⁺CD56⁺ 自然杀伤 (NK) 细胞增高的发生率 (80.6%, 29/36) 高于 ATA⁺ normal 组 (42.0%, 21/50), 差异有统计学意义 ($P=0.001$), CD3⁺CD4⁺ 辅助性 T(Th) 细胞降低的发生率 (41.7%, 15/36) 高于 ATA⁺ normal 组 (18.0%, 9/50), 差异有统计学意义 ($P=0.016$); ② ATA⁺ high 组 CD16⁺CD56⁺NK 细胞增高的发生率 (80.6%, 29/36) 高于 ATA⁻ high 组 (54.00%, 27/50), 差异有统计学意义 ($P=0.011$); CD3⁺CD4⁺Th 细胞降低的发生率 (41.7%, 15/36) 高于 ATA⁻ high 组 (20.0%, 10/50), 差异有统计学意义 ($P=0.029$); ③ ATA⁺ 组与 ATA⁻ 组比较, ATA⁺ normal 组与 ATA⁻ normal 组比较, ATA⁻ high 组与 ATA⁻ normal 组比较, 各淋巴细胞亚群异常 (增高/降低) 的发生率差异均无统计学意义 (P 值均 > 0.05)。**结论** ATA 阳性与轻度甲状腺功能受损同时存在时, 未孕的 RSA 患者细胞免疫状态存在异常, 推测 ATA 阳性合并轻度甲状腺功能受损时, RSA 的发生可能与免疫异常有关。

【关键词】 复发性流产; 抗甲状腺抗体; 淋巴细胞亚群

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· 临床研究 ·

Study of the relationship between antithyroid antibody and peripheral blood lymphocyte subsets in nonpregnant women with recurrent spontaneous abortion

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【Abstract】 Objective To find if anti-thyroid antibody (ATA) can be related with cellular immune status in unpregnant patients with recurrent spontaneous abortion (RSA), and its pathogenesis. **Methods** A total of 200 patients with RSA who were treated in Shengjing Hospital of China Medical University from December 2015 to December 2016 were enrolled for retrospective case-control study. According to the state of thyroid function, the patients were divided into two parts: ATA positive group (86 cases, ATA⁺ group), 36 cases of which thyroid stimulating hormone (TSH) ≥ 2.50 mIU/L, recording as ATA⁺ high group, 50 cases of which TSH < 2.50 mIU/L recording as ATA⁺ normal group; ATA negative group (114 cases, ATA⁻ group), 50 cases of which TSH ≥ 2.50 mIU/L recording as ATA⁻ high group, 64 cases of which TSH < 2.50 mIU/L recording as ATA⁻ normal group. The lymphocyte subsets and the thyroid function of each group were detected and the differences of lymphocyte subsets were analyzed between the groups. **Results** 1) The incidence of increased CD16⁺CD56⁺ natural killer (NK) cells of ATA⁺ high group (80.6%, 29/36) was significantly higher than that in ATA⁺ normal group (42.0%, 21/50) ($P=0.001$). The incidence of decreased CD3⁺CD4⁺ helper T (Th) cells of ATA⁺ high group (41.7%, 15/36) was significantly higher than that in ATA⁺ normal group (18.0%, 9/50) ($P=0.016$). 2) The incidence of increased CD16⁺CD56⁺ NK cells of ATA⁺ high group (80.6%, 29/36) was significantly higher than ATA⁻ high group (54.00%, 27/50) ($P=0.011$). The incidence of decreased CD3⁺CD4⁺Th cells of ATA⁺ high group (41.7%, 15/36) was significantly higher than that in ATA⁻ high group (20.0%, 10/50) ($P=0.029$). 3) Compared ATA⁺ group with ATA⁻ group, ATA⁺ normal group with ATA⁻ normal group, ATA⁻ high group with ATA⁻ normal group, there was no significant difference in the incidence of lymphocyte subsets abnormality (increase/decrease) ($P>0.05$). **Conclusion** Abnormal status of cellular immune status exists in RSA patients with both ATA and mild thyroid abnormalities, suggesting that the occurrence of RSA may be associated with immune factors when ATA and mild thyroid abnormalities coexist.

【Key words】 Recurrent spontaneous abortion; Anti-thyroid antibody; Lymphocyte subsets

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复发性流产中基质金属蛋白酶的调控机制研究

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【摘要】目的 探讨复发性流产(RSA)患者绒毛组织中基质金属蛋白酶(MMPs)的调控机制。方法 选取 2016 年 2—5 月期间就诊于苏州大学附属第一医院妇产科计划生育门诊的 RSA 患者 24 例为 RSA 组, 同期健康早孕流产患者 26 例为对照组, 酶联免疫吸附法(ELISA)检测血浆肿瘤坏死因子(TNF)- α 、白细胞介素(IL)-1 β 水平, 逆转录-聚合酶链式反应(RT-PCR)检测患者绒毛组织中 TNF- α 、IL-1 β 、核转录因子(NF)- κ B、核转录因子抑制蛋白(I κ B) β 、MMP-9 和 MMP-2 的 mRNA 表达情况, 采用蛋白印迹法检测分析 NF- κ B、I κ B β 、MMP-9、MMP-2 的蛋白表达。结果 ① RSA 组血浆中 TNF- α 水平为 $(2.84 \pm 0.62) \mu\text{g/L}$, 显著高于对照组的 $(1.32 \pm 0.43) \mu\text{g/L}$ ($P=0.047$)。② RSA 组绒毛组织中 TNF- α 、NF- κ B1、RelA、MMP-9 mRNA 相对表达量均高于对照组, 差异均有统计学意义 ($P<0.001$ 、 $P<0.001$ 、 $P=0.003$ 、 $P<0.001$), I κ B β mRNA 表达量显著低于对照组 ($P=0.011$); ③ RSA 组绒毛组织中 MMP-9、NF- κ B p65 和 p50 的蛋白表达水平均高于对照组, 差异均有统计学意义 ($P=0.001$ 、 $P=0.001$ 、 $P<0.001$), I κ B β 的蛋白表达水平显著低于对照组 ($P<0.001$)。结论 外周血中 TNF- α 水平的升高, 可影响绒毛组织中 I κ B 蛋白的降解, 活化 NF- κ B 使其表达水平升高, 进一步导致 MMP-9 表达升高, 从而引起蜕膜细胞外基质过度降解导致胚胎脱落, 最终导致流产发生。

【关键词】 自然流产; 绒毛组织; 基质金属蛋白酶; 复发性流产

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Regulatory mechanism of matrix metalloproteinases in recurrent spontaneous abortion

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【Abstract】 Objective To investigate the expression of matrix metalloproteinases (MMPs) in villi of patients with recurrent spontaneous abortion (RSA), and analyze the relationship and clinical significance between MMPs and RSA. **Methods** During February to May 2016 at Obstetrics and Gynecology, the First Affiliated Hospital of Soochow University, 24 patients with RSA were selected as RSA group, 26 healthy pregnant women in the same period were selected as control group, tumor necrosis factor (TNF)- α , interleukin (IL)-1 β levels in plasma were measured by enzyme linked immunosorbent assay (ELISA). IL-1 β , nuclear factor (NF)- κ B, inhibitor of tumor necrosis factor (I κ B) β , MMP-9 and MMP-2 were detected by RT-PCR, and the protein expression of MMP-9, MMP-2, NF- κ B and I κ B β were detected by Western blotting. **Results** 1) The level of TNF- α in plasma of RSA group [(2.84 \pm 0.62) μ g/L] was higher than that in control group [(1.32 \pm 0.43) μ g/L] ($P=0.047$). 2) The expressions of TNF- α , NF- κ B1, RelA and MMP-9 mRNA in villi of RSA group were significantly higher than those in control group ($P<0.001$, $P<0.001$, $P=0.003$, $P<0.001$), and the expression of I κ B β mRNA was significantly lower than that of control group ($P=0.011$). 3) The levels of MMP-9, NF- κ B p65 and p50 protein in villi were significantly higher than those in control group ($P=0.001$, $P=0.001$, $P<0.001$), and the level of I κ B β protein in villi was significantly lower than that in control group ($P<0.001$). **Conclusion** The increase of TNF- α level in peripheral cells can affect the degradation of the protein of I κ B in villi. The elevated expression of NF- κ B increases the level of MMP-9, the excessive degradation of extracellular matrix in decidua leads to the shedding of embryo, and may induce miscarriage eventually.

【Key words】 Spontaneous abortion; Chorionic villi; Matrix metalloproteinases; Recurrent spontaneous abortion

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纳米银对小鼠睾丸组织结构和细胞凋亡的影响及与线粒体和 DNA 损伤关系的研究

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【摘要】目的 观察纳米银对小鼠睾丸组织结构和细胞凋亡的影响, 并探讨其有关机制。方法 体内实验: 15 只雄性 Balb/c 小鼠分为阴性对照组、低剂量组 [30 mg/(kg·d)]、高剂量组 [125 mg/(kg·d)], 阴性对照组未做干预, 低剂量组和高剂量组用纳米银混悬液连续灌胃 90 d。HE 染色及末端转移酶标记技术 (TUNEL) 测定小鼠睾丸组织病理学改变及细胞凋亡情况, 抽血测定生殖激素, 分离附睾测定精子浓度及精子活力。体外实验: 取对数生长期的鼠精原细胞系 (GC2), 用不同浓度纳米银干预 (Ctrl、5 mg/L、10 mg/L、20 mg/L、40 mg/L 和 80 mg/L) 24 h 后, 观察细胞形态, CCK8 法检测细胞活性, 流式细胞仪检测细胞凋亡情况, 电子显微镜下观察纳米银沉积和线粒体结构, 免疫荧光检测 DNA 损伤情况。结果 与阴性对照组相比, 高剂量纳米银导致睾丸组织排列紊乱、间隙增宽, 细胞凋亡比率明显增加, 小鼠精子浓度降低、活力下降; 体外研究显示, 20 mg/L 以上纳米银干预后 GC2 细胞生长明显受抑, 细胞凋亡率比阴性对照组显著增加 (P 均 <0.05), 且线粒体结构异常, DNA 损伤特异蛋白 (γ H2AX) 染色明显增强。结论 高剂量纳米银可导致小鼠睾丸组织结构异常和细胞凋亡率增加, 可能与纳米银导致线粒体结构异常和 DNA 损伤有关。

【关键词】 纳米银; 睾丸组织; 凋亡; DNA 损伤; 线粒体

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· 实验研究 ·

Effect of nanosilver on mouse tissue structure and apoptosis, and its relationship with mitochondria and DNA damage

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【Abstract】 Objective To observe the effect of nanosilver on the testicular tissue structure and cells apoptosis in mice and to explore its mechanism. **Methods** *In vivo* experiments: 15 male Balb/c mice were divided randomly into negative control group, low dose group [30 mg/(kg·d)] and high dose group [125 mg/(kg·d)]. Negative control group was not intervened, while low dose group and high dose group were given by gavage for 90 d. The testicular histopathological changes and cell apoptosis were determined by HE staining and TUNEL assay. Blood was drawn to detect reproductive hormones, and epididymis was isolated to detect sperm concentration and sperm motility. *In vitro* experiments: mouse spermatogonial cells (GC2) grown in logarithmic phase were treated with various concentrations of nanosilver (Ctrl, 5 mg/L, 10 mg/L, 20 mg/L, 40 mg/L and 80 mg/L). Then cell morphologies were observed. Cell viability were detected by CCK8 assay. Apoptosis were detected by flow cytometry. Nanosilver deposition and mitochondrial structure were observed under electron microscope. DNA damage was detected by immunofluorescence. **Results** Compared with negative control group, the high dose of nanosilver resulted in disorganized testicular tissue, broaden gap, a significant increase in the apoptotic rate of spermatogonia, reduced sperm concentration and viability. *In vitro* studies showed that the growth of GC2 cells was significantly inhibited and the apoptotic rate of GC2 cells was significantly increased after intervention with nanosilver above 20 mg/L ($P<0.05$). Accompanied with the abnormal structure of mitochondria, DNA damage-specific protein (γ H2AX) staining obviously increased. **Conclusion** High dose of nanosilver can cause testicular tissue structure abnormal and increase apoptotic rate of GC2 cells in mice, which may due to the fact that nanosilver cause abnormalities in mitochondrial structure and DNA damage.

【Key words】 Nanosilver; Testicular tissue; Apoptosis; DNA damage; Mitochondria

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褪黑素对卵巢过度刺激综合征小鼠的影响

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【摘要】 目的 探讨褪黑素对卵巢过度刺激综合征 (OHSS) 的预防作用。方法 将小鼠随机分为促排卵组 (CS)、过度刺激组 (OS)、低剂量褪黑素组 (LM)、中剂量褪黑素组 (MM) 和高剂量褪黑素组 (HM) 共 5 组, 其中 OS、LM、MM 和 HM 4 组采用 10 IU 孕马血清促性腺激素 (PMSG) 联合 30 IU 人绒毛膜促性腺激素 (hCG) 法建立 OHSS 小鼠模型, 在建模期间分别对 LM、MM 和 HM 组注射低、中和高浓度 (10 mg/kg、20 mg/kg 和 40 mg/kg) 的褪黑素。比较各组间卵巢体比、腹腔毛细血管通透性、卵巢中囊性纤维化跨膜转运调节因子 (cfr)、血管内皮生长因子 (vegf) 及其受体 (kdr) 的 mRNA 表达水平、血清中雌二醇 (E₂)、黄体生成素 (LH)、催乳素 (PRL) 和血管紧张素 II (AII) 的含量。结果 ① OS 组的卵巢体比 (0.228%±0.023%)、腹腔毛细血管通透性 [(1.722±0.248) g/L]、vegf mRNA 表达水平 (470.94±132.43)、血清中 E₂ [(188.81±16.40) ng/L] 和 AII 的含量 [(919.36±62.39) ng/L] 显著高于 CS 组 [0.120%±0.012%、(0.892±0.221) g/L、1.32±0.54、(17.84±1.20) ng/L、(173.65±20.60) ng/L] (*P*<0.05); ② HM 组的卵巢体比 (0.169%±0.004%)、腹腔毛细血管通透性 [(0.650±0.228) g/L]、vegf mRNA 表达水平 (10.36±3.92)、血清中 E₂ [(66.78±15.16) ng/L] 和 AII [(399.12±37.60) ng/L] 的含量显著低于 OS 组 [0.228%±0.023%、(1.722±0.248) g/L、470.94±132.43、(188.81±16.40) ng/L、(919.36±62.39) ng/L] (*P*<0.05); ③ HM 组的腹腔毛细血管通透性、vegf mRNA 表达水平和血清中 E₂ 的含量与 CS 组间差异无统计学意义 (*P*>0.05)。结论 OHSS 小鼠建模成功, 高浓度的褪黑素可抑制 OHSS 诱发的卵巢增大、血管通透性增加, 降低卵巢中 vegf mRNA 表达水平、血清中 E₂ 和 AII 的含量, 有望缓解 OHSS 的症状。

【关键词】 卵巢过度刺激综合征; 褪黑素; 预防; OHSS 小鼠模型

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Effect of melatonin on ovarian hyperstimulation syndrome mouse model

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【Abstract】 Objective To investigate the preventive effect of melatonin on ovarian hyperstimulation syndrome (OHSS) in OHSS mouse model. **Methods** The mice were randomly assigned to 5 groups: the induced ovulation group (CS), the over stimulation group (OS), the low dose of melatonin group (LM), the middle dose of melatonin group (MM) and the high dose of melatonin group (HM). In OS, LM, MM and HM groups, the OHSS mouse model was built by pregnant mare serum gonadotropin and human chorionic gonadotrophin (PMSG-hCG) method. And the low dose (10 mg/kg), medium dose (20 mg/kg) and high dose (40 mg/kg) of melatonin were injected into mice in LM, MM and HM groups respectively during the OHSS modeling. The ovarian index, the peritoneal capillary permeability, the mRNA expression of cystic fibrosis transmembrane conductance regulator (cfr), vascular endothelial growth factor (vegf) and its receptor kdr in ovaries, the levels of estradiol (E₂), luteinizing hormone (LH), prolactin (PRL) and angiotensin II (AII) in serum were compared among these groups respectively. **Results** 1) The ratio of ovarian weight to body weight ($0.228\% \pm 0.023\%$), the peritoneal capillary permeability [(1.722 ± 0.248) g/L], the *vegf* mRNA expression (470.94 ± 132.43), the levels of E₂ [(188.81 ± 16.40) ng/L] and AII [(919.36 ± 62.39) ng/L] in serum of OS group were significantly higher than those of CS group [$0.120\% \pm 0.012\%$, (0.892 ± 0.221) g/L, 1.32 ± 0.54 , (17.84 ± 1.20) ng/L, (173.65 ± 20.60) ng/L] ($P < 0.05$). 2) The ratio of ovarian weight to body weight ($0.169\% \pm 0.004\%$), the peritoneal capillary permeability [(0.650 ± 0.228) g/L], the *vegf* mRNA expression (10.36 ± 3.92), the levels of E₂ [(66.78 ± 15.16) ng/L] and AII [(399.12 ± 37.60) ng/L] in serum of HM group were significantly lower than those of OS group [$0.228\% \pm 0.023\%$, (1.722 ± 0.248) g/L, 470.94 ± 132.43 , (188.81 ± 16.40) ng/L, (919.36 ± 62.39) ng/L] ($P < 0.05$). 3) The peritoneal capillary permeability, the *vegf* mRNA expression and the levels of E₂ in serum of HM group were not significantly different from CS group ($P > 0.05$). **Conclusion** The OHSS mouse model was built successfully. High concentration of melatonin inhibited OHSS-induced ovarian enlargement and increased vascular permeability, reduced the *vegf* mRNA expression in ovary and the levels of E₂ and AII in serum to alleviate the symptoms of OHSS.

【Key words】 Ovarian hyperstimulation syndrome; Melatonin; Prevention; OHSS mice model

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妊娠意愿量表的信效度评价

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【摘要】目的 对初步开发的妊娠意愿量表信效度进行评价, 以了解该量表在当前中国背景下, 测量女性妊娠意愿的可靠性及有效性。**方法** 在定性研究构建好的妊娠意愿概念模型基础上, 形成预试量表, 并对 2016 年 8 月 20 日—11 月 25 日期间在湖北省 2 家地市级妇幼保健院进行孕检、产后访视或行人工流产手术的 438 名女性进行调查。量表信度使用 Cronbach's α 系数和条目与总分间相关系数进行评价; 结构效度评价采用探索性因子分析和研究假设验证。**结果** 研究最后形成了含 12 个条目的妊娠意愿量表, 女性妊娠意愿的强弱和计划状态通过一系列分值呈现 (0~24)。量表 Cronbach's $\alpha=0.777$, 各条目与量表总分相关系数均 >0.2 。结构效度较好, 因子分析共提取 3 个公因子, 累积方差贡献率为 51.86%, 且各条目在其公因子上的因子载荷均 >0.4 , 量表得分分布满足所有研究假设。**结论** 该量表对于妊娠意愿的测量是可靠的、有效的, 易于被中国女性接受。该量表能够定量评价多种不同妊娠状态女性的妊娠意愿, 加强我们对中国妇女妊娠意愿的理解, 从而更好地为妇女避孕、计划生育、生殖健康提供服务。

【关键词】 妊娠意愿; 量表; 信度; 效度

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Evaluation on reliability and validity of pregnancy intention scale

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【Abstract】 Objective To evaluate the reliability and validity of the pregnancy intention scale which can be used in different pregnancy status in the context of contemporary China. **Methods** On the basis of the conceptual model of pregnancy intention developed by qualitative research, the measurement of unplanned intention was preliminary established. A total of 438 samples including pregnant (continuing pregnancy and seeking for abortion) and postnatal women recruited from two maternal and child health hospitals in Hubei Province from August 20 to November 25, 2016 were surveyed. Internal consistency was assessed using the Cronbach's α Statistic and item-total correlation coefficient, and construct validity was assessed using exploratory factor analysis and hypothesis testing. **Results** A twelve item measure of pregnancy intention was produced, women's pregnancy intention/planning was represented by the range of scores (0–24). The Cronbach's α coefficient of the scale was 0.777, and all item-total correlations were >0.2 . Three factors were extracted through exploratory factor analysis, the cumulative variance contribution rate was 51.86%, and all items' factor loadings were >0.4 . All hypotheses to test construct validity were met. **Conclusion** The pregnancy intention scale was reliable, valid, and acceptable for Chinese women. The scale can be used as an effective tool for improving our understanding, quantitative measurement and evaluation of women's pregnancy intention, thus providing better contraception, family planning, and reproductive health service to women.

【Key words】 Pregnancy intention; Scale; Reliability; Validity

Fund program: Hubei Province Health and Family Planning Scientific Research Project (WJ2017M007)

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宫腔灌注人绒毛膜促性腺激素对冻融胚胎移植结局影响的 Meta 分析

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【摘要】 目的 分析人绒毛膜促性腺激素(hCG)宫腔灌注对冻融胚胎移植(frozen-thawed embryo transfer, FET)周期临床结局的影响。方法 检索 Pubmed、EMbase、Cochrane Library、Web of Science、中国知网数据库、万方数据库和 CBM 文献, 检索时限截止至 2018 年 1 月 1 日。纳入 FET 周期中行 hCG 宫腔灌注相关的原始研究。由 2 名研究者独立进行文献筛选、资料提取并评价纳入研究的偏倚风险后, 采用 RevMan5.3 软件进行分析。结果 8 篇研究符合纳入标准, 共计 1823 个周期, 其中实验组 819 个周期, 对照组 1004 个周期。经分析, 试验组胚胎种植率($OR=1.41$, 95% $CI=1.04\sim 1.91$, $P=0.03$, $I^2=0\%$)、临床妊娠率($OR=1.56$, 95% $CI=1.26\sim 1.94$, $P<0.000 1$, $I^2=12\%$)和持续妊娠率($OR=2.41$, 95% $CI=1.37\sim 4.21$, $P=0.002$, $I^2=31\%$)显著高于对照组, 生化妊娠率($OR=1.88$, 95% $CI=0.85\sim 4.17$, $P=0.12$, $I^2=0\%$)与自发流产率($OR=0.67$, 95% $CI=0.33\sim 1.35$, $P=0.26$, $I^2=0\%$)组间差异无统计学意义。结论 hCG 宫腔灌注可以提高不孕患者 FET 周期的胚胎种植率、临床妊娠率和持续妊娠率, 对其妊娠结局具有改善作用。

【关键词】 人绒毛膜促性腺激素; 宫腔灌注; 冻融胚胎移植; Meta 分析

基金项目: 甘肃省卫生行业项目(GSWSKY-2015-47)

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Intrauterine injection human chorionic gonadotropin before the frozen-thawed embryo transfer: a Meta-analysis

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【Abstract】 Objective To evaluate the effect of intrauterine injection of human chorionic gonadotropin (hCG) on frozen-thawed embryo transfer (FET) outcomes. **Methods** Pubmed, EMBASE, Cochrane library, Web of Science, Wanfang database, CNKI and CBM were searched from inception to January 2018. Relevant clinical studies which investigated the effect of intrauterine injection of hCG on FET outcomes were included. Two investigators independently accomplished articles screening, data extraction and quality assessment, then, statistical analyses were performed by RevMan5.3. **Results** A total of 8 studies were included with 1823 cycles, of which, 819 cycles were in experimental group while 1004 cycles were in control group. The Meta-analysis showed that the experimental group had significantly higher implantation rate ($OR=1.41$, 95% $CI=1.04-1.91$, $P=0.03$, $I^2=0\%$), clinical pregnancy rate ($OR=1.56$, 95% $CI=1.26-1.94$, $P<0.0001$, $I^2=12\%$) and ongoing pregnancy rate ($OR=2.41$, 95% $CI=1.37-4.21$, $P=0.002$, $I^2=31\%$) than control group. And higher biochemical pregnancy rate ($OR=1.88$, 95% $CI=0.85-4.17$, $P=0.12$, $I^2=0\%$) and less spontaneous abortion rate ($OR=0.67$, 95% $CI=0.33-1.35$, $P=0.26$, $I^2=0\%$) were found in experimental group, but there were no significantly statistical differences. **Conclusion** Our Meta-analysis indicated that intrauterine injection of hCG could improve implantation rate, clinical pregnancy rate and ongoing pregnancy rate of FET cycles. In addition, intrauterine injection hCG before FET is beneficial to the pregnancy outcomes.

【Key words】 Human chorionic gonadotropin; Intrauterine injection; Frozen-thawed embryo transfer; Meta-analysis

Fund program: Health Industry Project of Gansu Province (GSWSKY-2015-47)

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两种剂量芬吗通在中、重度宫腔粘连患者中的疗效分析

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【摘要】 目的 探讨两种剂量芬吗通在中、重度宫腔粘连患者治疗中的疗效。方法 选取 2015 年 1—9 月期间在本院经宫腔镜检查、按美国生育协会 (AFS) 评分标准诊断为中、重度宫腔粘连患者 60 例, 按用药方法分成 A、B 组, 每组 30 例, 所有患者均在宫腔镜下行宫腔粘连分离术, 术后补充雌激素治疗 3 个月, A 组给予芬吗通 1 mg/d, 阴道给药, B 组给予芬吗通 2 mg/d, 阴道给药, 用药前后均检测血雌二醇 (E_2) 及监测内膜厚度, 用药期间定期随访药物不良反应, 3 个月后行宫腔镜二探术, 了解宫腔恢复情况。结果 A 组中、重度宫腔粘连患者用药后血 E_2 分别升至 (501.67 ± 127.04) ng/L 及 (550.38 ± 135.46) ng/L, 内膜厚度分别增至 (7.01 ± 0.57) mm 及 (6.28 ± 0.51) mm, B 组中、重度宫腔粘连患者用药后血 E_2 分别升至 $(1\ 099.70 \pm 97.88)$ ng/L 及 $(1\ 196.25 \pm 169.56)$ ng/L, 内膜厚度分别增至 (6.65 ± 0.60) mm 及 (5.70 ± 0.47) mm, B 组用药后 E_2 升高较 A 组明显 ($P < 0.001$), 在中度粘连患者中内膜增长组间差异无统计学意义 ($P > 0.05$), 而在重度宫腔粘连患者中 B 组的 E_2 升高明显 ($P < 0.001$), 内膜厚度增长不如 A 组 ($P = 0.019$); 在临床疗效方面组间差异无统计学意义 ($P > 0.05$), 但 B 组的药物不良反应较 A 组明显增多。结论 对于重度宫腔粘连患者不可盲目加大雌激素用量, 因其并不能明显增加子宫内膜厚度、提高临床疗效, 且有增加药物不良反应的风险。

【关键词】 宫腔粘连; 芬吗通; 激素补充疗法

基金项目: 厦门市科技计划项目 (3502Z20154044)

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Effect analysis of different levels of femoston on moderate and severe intrauterine adhesions

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【Abstract】 Objective To investigate the effect of femoston with two doses in the treatment of moderate and severe intrauterine adhesions. **Methods** Sixty patients with moderate and severe intrauterine adhesions were confirmed by hysteroscopy examination and American Fertility Society (AFS) grading standard. They were divided into group A and group B according to different applications femoston, each group with 30 cases. All patients were treated with transcervical resection of adhesion and received estrogen treatment for 3 months. In group A, 30 cases were all given femoston 1 mg/d. In group B, 30 cases were given femoston 2 mg/d. All patients before and after taking medications were drawn blood to test estradiol (E_2) and given an ultrasound examination to measure the endometrial thickness. The adverse reactions of drug were followed up regularly during the treatment, hysteroscopy once again to evaluate uterine cavity after 3 months. **Results** In group A, the concentrations of E_2 in serum of moderate and severe intrauterine adhesions risen to (501.67 ± 127.04) ng/L and (550.38 ± 135.46) ng/L, respectively, endometrium thickness was increased to (7.01 ± 0.57) mm and (6.28 ± 0.51) mm. In group B, the concentrations of estradiol in serum of moderate and severe intrauterine adhesions risen to $(1\ 099.70 \pm 97.88)$ ng/L and $(1\ 196.25 \pm 169.56)$ ng/L, endometrium thickness was increased to (6.65 ± 0.60) mm and (5.70 ± 0.47) mm. The concentrations of E_2 in serum of group B were significantly higher than that in group A ($P < 0.001$). The difference of endometrium thickness in two groups with moderate adhesion was not statistically significant ($P > 0.05$). In severe intrauterine adhesion, the endometrium thickness of group A was better than group B ($P < 0.001$), in which the concentration of E_2 in serum was higher ($P = 0.019$). That was no significant difference between the two groups in clinical effect ($P > 0.05$), and the adverse reactions of drug in group B increased obviously compared with group A. **Conclusion** The patients with severe intrauterine adhesions cannot increase the dosage of estrogen blindly, because it cannot increase endometrial thickness and improve the clinical effect significantly, but increase the adverse reactions of drug.

【Key words】 Intrauterine adhesions; Femoston; Hormone supplement therapy

Fund program: Xiamen Science and Technology Project (3502Z20154044)

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卵泡液透明质酸水平与卵巢低储备人群 获卵结果的相关性分析

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【摘要】目的 分析卵巢低储备患者卵泡液中透明质酸水平与取卵结果的相关性。方法 测定 34 个未获卵卵泡液(研究组)和 39 个获卵卵泡液(对照组)的透明质酸和孕酮等指标,并测定人群血清抗苗勒管激素(AMH)。结果 研究组血清 AMH $[(0.55 \pm 0.37) \mu\text{g/L}]$ 水平低于对照组 $[(0.75 \pm 0.42) \mu\text{g/L}]$, $P=0.033$, 卵泡液透明质酸浓度 $[(274 \pm 65) \mu\text{g/L}]$ 低于对照组 $[(347 \pm 86) \mu\text{g/L}]$, $P<0.001$, 孕酮水平 $[(91.4 \pm 25.3) \times 10^3 \text{ nmol/L}]$ 水平高于对照组 $[(81.3 \pm 15.6) \times 10^3 \text{ nmol/L}]$, $P=0.042$ 。结论 卵巢低储备人群获卵失败与卵泡液透明质酸不足存在相关性。

【关键词】卵泡液; 抗苗勒管激素(AMH); 透明质酸; 卵巢储备

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· 临床报道 ·

Correlation between hyaluronic acid in follicular fluid and oocyte retrieval outcome in patients with diminished ovarian reserve

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【Abstract】 Objective To analyze the correlation between the concentration of hyaluronic acid in follicular fluid and oocyte retrieval results in the patients with diminished ovarian reserve. **Methods** The concentration of anti-Müllerian hormone (AMH) in serum, hyaluronic acid and progesterone in follicular fluid of 34 patients with none oocytes retrieved (study group) and 39 patients with successful retrieval (control group) were measured and compared. **Results** The concentration of AMH level $[(0.55 \pm 0.37) \mu\text{g/L}]$ in serum and hyaluronic acid $[(274 \pm 65) \mu\text{g/L}]$ in follicular fluid were lower than that in control group $[(0.75 \pm 0.42) \mu\text{g/L}, P=0.033; (347 \pm 86) \mu\text{g/L}, P<0.001]$. The level of progesterone in follicular fluid $[(91.4 \pm 25.3) \times 10^3 \text{ nmol/L}]$ was higher than that in control group $[(81.3 \pm 15.6) \times 10^3 \text{ nmol/L}, P=0.042]$. **Conclusion** The failure of oocytes retrieval in diminished ovarian reserver is related to the insufficiency of hyaluronic acid in follicular fluid.

【Key words】 Follicular fluid; Anti-Müllerian hormone (AMH); Hyaluronic acid; Ovarian reserve

Fund program: Medical and Health Science and Technology Plan Project of Zhejiang Province (2017KY219); Zhejiang Provincial Natural Science Foundation of China (LY15H260004)

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二甲双胍对中心性肥胖和非中心性肥胖多囊卵巢综合征患者生殖内分泌及糖脂代谢的影响

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【摘要】目的 探讨二甲双胍在中心性肥胖和非中心性肥胖多囊卵巢综合征(PCOS)患者治疗中的适应证。方法 以腰围 80 cm 为界, 将 2016 年 1 月—2018 年 4 月期间来复旦大学附属妇产科医院就诊的 113 例 PCOS 患者分为中心性肥胖组(腰围 \geq 80 cm)和非中心性肥胖组(腰围 $<$ 80 cm), 给予二甲双胍(1.5 g/d)治疗 3 个月。记录治疗前后患者身高、体质量、腰围及月经周期, 收集外周血测定治疗前后生殖内分泌和糖脂代谢指标。结果 治疗后, 中心性肥胖组和非中心性肥胖组的排卵率分别为 59.7% 和 56.1%, 月经周期改善率分别为 83.8% 和 84.2%, 组间差异均无统计学意义($P>0.05$)。治疗后, 中心性肥胖组和非中心性肥胖组内分泌指标中黄体生成素(LH)、总睾酮(TT)、游离雄激素指数(FAI)均较治疗前显著下降($P<0.05$); 糖代谢指标中, 空腹血糖(FPG)、空腹胰岛素(FINS)和胰岛素抵抗指数(HOMA-IR)均较治疗前显著下降($P<0.05$), 但仅中心性肥胖组胰岛素曲线下面积(IAUC)较治疗前显著下降($P<0.05$); 脂代谢指标中, 体质量指数(BMI)和腰围均改善($P<0.05$), 且肥胖组载脂蛋白 A(APO-A)显著上升($P<0.05$)。结论 二甲双胍不仅适用于中心性肥胖 PCOS 患者, 同样适用于非中心性肥胖 PCOS 患者。

【关键词】多囊卵巢综合征; 二甲双胍; 中心性肥胖; 月经周期; 糖脂代谢

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Effect of metformin on reproductive endocrine and glucose and lipid metabolism of polycystic ovary syndrome patients with or without central obesity

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【Abstract】 Objective To explore the therapeutic status of metformin in central obesity and non-central obesity polycystic ovary syndrome (PCOS) patients. **Methods** Totally 113 PCOS patients of Obstetrics and Gynecology Hospital, Fudan University from January 2016 to April 2018 were divided into central obesity group (waist circumference ≥ 80 cm) and non-central obesity group (waist circumference < 80 cm) according to waist circumference. They were treated with metformin (1.5 g/d) for 3 months. The height, weight, waist circumference and menstrual cycle were recorded before and after treatment. Peripheral blood was taken to measure reproductive endocrine and glucose and lipid metabolism indexes before and after treatment. **Results** After treatment, the ovulation rates of central obese and non-central obesity groups were 59.7% and 56.1%, respectively, and there was no statistical difference between the two groups ($P > 0.05$). The improvement rates of menstrual cycle in central obese and non-central obesity groups were 83.8% and 84.2%, respectively, with no statistical difference between the two groups ($P > 0.05$). After treatment, luteinizing hormone (LH), total testosterone (TT), and free androgen index (FAI) decreased significantly in central obese and non-central obesity groups ($P < 0.05$). Fasting plasma glucose (FPG), fast insulin (FINS) and homeostasis model assessment of insulin resistance (HOMA-IR) in both groups significantly decreased ($P < 0.05$), but only insulin area under the curve (IAUC) in central obesity group significantly decreased ($P < 0.05$). Body mass index (BMI) and waist circumference decreased in the two groups ($P < 0.05$). However, only apolipoprotein A (APO-A) in central obese group increased significantly ($P < 0.05$). **Conclusion** Metformin is not only suitable for central obese PCOS patients, but also for non-central obese PCOS patients.

【Key words】 Polycystic ovary syndrome; Metformin; Central obesity; Menstrual cycle; Glucose and lipid metabolism

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非嵌合型克氏综合征患者经显微取精术获得临床妊娠的 1 例病例报道

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【摘要】 目的 探究非嵌合型克氏综合征患者通过辅助生殖技术 (ART) 获得自己遗传学后代的可能性。方法 一对夫妇因女方原发性不孕、右侧输卵管梗阻, 男方多次精液常规检查示无精子, 染色体 47,XXY, 诊断为克氏综合征, 要求行 ART 助孕, 给予女方超促排卵治疗, 并于取卵当日男方行睾丸切开显微取精术, 成功获得精子, 结合卵胞质内单精子注射 (intracytoplasmic sperm injection, ICSI) 技术获得可用胚胎。结果 该不孕夫妇经睾丸显微取精术成功获得精子, 经 ICSI 受精后, 受精率为 76.19%(16/21), 获优质胚胎 6 枚、囊胚 7 枚, 行冻融胚胎移植 (FET) 后成功妊娠。结论 睾丸切开显微取精术可成为非嵌合型克氏综合征患者实现生育自己遗传学后代的可能。

【关键词】 克氏综合征; 睾丸切开显微取精术; 卵胞质内单精子注射

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Successful clinical pregnancy derived from microdissection testicular sperm extraction in a patient with nonmosaic Klinefelter syndrome: a case report

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【Abstract】 Objective To explore the possibility of obtaining genetic offspring through emerging assisted reproductive technology in patients with nonmosaic Klinefelter syndrome. **Methods** The wife was primary infertility, with the right oviduct obstruction, the husband's semen revealed no sperm, chromosome 47,XXY was diagnosed as Klinefelter syndrome. Assisted reproductive technology was required and sperm was successfully retrieved through microdissection testicular sperm extraction (micro-TESE) on the day of his wife got oocytes picked up. Embryos were obtained by intracytoplasmic sperm injection (ICSI) technology. **Results** The sperm was successfully retrieved through micro-TESE and fertility rate was 76.19% (16/21) by ICSI. Six high-quality embryos and 7 blastocysts were retrieved. Clinical pregnancy was obtained after frozen-thawed embryo transfer. **Conclusion** Micro-TESE can become possible for patients with nonmosaic Klinefelter syndrome to produce their own genetic offsprings.

【Key words】 Klinefelter syndrome; Microdissection testicular sperm extraction; Intracytoplasmic sperm injection

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不明原因复发性自然流产的孕激素治疗进展

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【摘要】对不明原因复发性自然流产，目前的干预治疗欠针对性，还没有确认有效的确切治疗措施，如何使这部分人群获益是目前生殖领域的一大难题。孕激素对妊娠的维持至关重要。然而，在妊娠 12 周前添加口服孕激素是否将增加有不明原因复发性自然流产史的妇女的活产率尚不确定，但这一研究具有重要的临床实用价值。本文重点关注孕激素类药物和孕激素类药物治疗不明原因复发性自然流产患者的临床研究进展，以期为今后临床治疗方案和研究方向提供思路。

【关键词】不明原因复发性自然流产；孕激素；治疗进展

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Advances in treatment of progesterone on unexplained recurrent pregnancy loss

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【Abstract】 For unexplained recurrent pregnancy loss (URPL), the current therapeutic interventions is not targeted, and no effective and definitive medical treatment have been identified. How to benefit this group of women is a major problem in the field of reproduction at present. Progesterone is important for the maintenance of pregnancy. However, it is uncertain whether the addition of oral progesterone in the first trimester will increase the live birth rate of women with the history of URPL. But it is important for our clinical practice. This article focuses on the recent clinical trial of progesterone for treatment of URPL, in order to provide ideas for clinical practice and research in the future.

【Key words】 Unexplained recurrent pregnancy loss; Progesterone; Advances in treatment

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植入前遗传学检测技术的现状及新进展

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【摘要】 随着辅助生殖技术的发展, 植入前遗传学检测 (preimplantation genetic testing, PGT) 技术获得了越来越多的临床应用和关注。植入前遗传学诊断 (preimplantation genetic diagnosis, PGD) 的目的是避免遗传相关的染色体相关疾病的发生, 而随着人们对着床率、活产率等要求逐渐提高, 植入前遗传学筛查 (preimplantation genetic screening, PGS) 应运而生, 即避免非整倍体胚胎移植流产以及反复胚胎染色体异常所导致的复发性流产。随着 PGT 的普及, 生殖医学从业者需要对该技术进行充分的认识, 以帮助患者更好地解决临床问题。本文回顾了 PGT 在近 30 年发展过程中活检技术、检测技术方面的发展, 并总结了不同时期活检的妊娠结局, 对 PGT 技术的安全性进行了评估。同时, 我们还对 PGT 技术当前存在的问题进行了分析, 并对其未来的发展方向进行了展望。

【关键词】 植入前遗传学检测; 妊娠结局; 检测技术; 活检技术

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Current status and new progress of the preimplantation genetic testing

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【Abstract】 With the development of assisted reproduction technique, preimplantation genetic testing (PGT) has gained more clinical application and more attention. Preimplantation genetic diagnosis (PGD), is used to avoid genetic diseases obtained from parents. With the improving of the demand of higher implantation rate and live birth rate, preimplantation genetic screening (PGS) is brought up to avoid aneuploidy, which can lead to adverse pregnancy outcomes. With the widespread of the PGT, we have to get a comprehensive understanding of the technique, so as to help patients to solve the clinical problems. In this review, we retrospect the development of the biopsy techniques and the testing techniques of PGT within nearly 30 years, and summarize the different pregnancy outcomes of blastomere biopsy and trophoctoderm cells biopsy to assess the security of PGT. In addition, we analyze the current problems of PGT, and discuss its prospect in the future.

【Key words】 Preimplantation genetic testing; Pregnancy outcomes; Testing technique; Biopsy technique

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高通量测序及单细胞分离技术在无创产前诊断中的应用

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【摘要】 孕妇血浆中胎儿游离 DNA(cell-free fetal DNA, cff DNA) 的发现, 以及胎儿游离细胞 (有核红细胞、滋养层细胞) 分离技术的成熟, 为无创产前诊断 (non-invasive prenatal testing, NIPT) 提供了广阔的前景。借助各种分子诊断技术, 对 cff DNA 或游离细胞进行胎儿染色体疾病和单基因遗传病的研究迅速成为热点。本文对 cff DNA 的发现、高通量测序技术 (high-throughput sequencing) 和胎儿游离细胞在无创产前诊断中的应用进行了综述。

【关键词】 胎儿游离 DNA; 高通量测序技术; 染色体非整倍体疾病; 单基因遗传病; 无创产前诊断

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Application of high-throughput sequencing in non-invasive prenatal testing

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【Abstract】 The discovery of cell-free fetal DNA (cff DNA) in maternal plasma, as well as the maturation of fetal cell (nucleated red blood cells and trophoblast cells) separation techniques provides a broad prospect for non-invasive prenatal testing (NIPT). A variety of molecular diagnostic techniques had been developed to diagnose fetal chromosomal abnormalities and monogenic diseases. This article will review the discovery of cff DNA, the application of high-throughput sequencing and fetal cell in non-invasive prenatal testing.

【Key words】 Cell-free fetal DNA; High-throughput sequencing; Chromosome aneuploidy; Monogenic disease; Non-invasive prenatal testing

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多囊卵巢综合征与氧化应激相关性研究进展

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【摘要】 多囊卵巢综合征 (polycystic ovary syndrome, PCOS) 是女性最常见的内分泌紊乱疾病, 影响全球 4%~12% 育龄期女性的生殖健康, 是导致女性发生不孕最常见的因素之一。PCOS 病因复杂且发病机制未完全明确, 在众多致病因素中, 氧化应激 (OS) 被认为是 PCOS 发病的因素之一, 且与其临床症状的发生及进展有密切关系。循环中异常增高的 OS 产物还会导致该类患者发生心脑血管疾病、肝病、肿瘤的风险上升, 甚至影响子代的健康。因此, OS 在 PCOS 患者病情的进展中起至关重要的作用。本文就 OS 在 PCOS 患者相关临床症状中的发病机制做一简要综述。

【关键词】 氧化应激; 多囊卵巢综合征; 心血管疾病; 子代

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Research progress on the correlation between polycystic ovary syndrome and oxidative stress

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【Abstract】 Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women, affecting the reproductive health of 4%–12% women with childbearing age worldwide, and is one of the most common factors leading to infertility in women. The etiology of PCOS is complex and the pathogenesis is not completely clear. Among the many pathogenic factors, oxidative stress is considered to be one of the factors in the pathogenesis of PCOS, and it is closely related to the occurrence and progression of clinical symptoms. The abnormally elevated oxidative stress products in the circulation can also lead to an increased risk of cardiovascular and cerebrovascular diseases, liver diseases, and tumors in such patients, and even affect the health of the offspring. Therefore, oxidative stress plays a crucial role in the progression of PCOS patients. This article provides a brief review of the pathogenesis of oxidative stress in clinical symptoms associated with PCOS patients.

【Key words】 Oxidative stress; Polycystic ovary syndrome; Cardiovascular disease; Offspring

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脆性 X 综合征相关基因与卵巢功能相关分子机制研究进展

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【摘要】 脆性 X 智力低下 (fragile X mental retardation 1, FMR1) 基因已被证实是导致原发卵巢功能不足 (primary ovarian insufficiency, POI) 和卵巢储备功能减退 (diminished ovarian reserve, DOR) 最重要的单基因, 其突变将导致脆性 X 相关的原发性卵巢功能不全——脆性 X 相关的卵巢储备功能降低 (FXDOR) 和脆性 X 相关的原发卵巢功能不足 (FXPOI)。FMR1 前突变携带者患有 POI 的风险高达 20%, 散发的 POI 患者中 FMR1 前突变携带者为 0.8%~13%。目前 FXDOR 和 FXPOI 的发病分子机制仍不清楚, 研究表明可能与 FMR1 mRNA 过度堆积、脆性 X 智力低下蛋白 (FMRP) 相关 mRNA 调节异常、FMRpolyG 内含子的泛素化调节、FMR1 基因组蛋白修饰改变以及 FMR1 引起的卵泡发育相关分子及通路的异常表达相关。本文以卵巢功能相关 FMR1 基因为中心, 对其引起卵巢功能不全的相关分子机制研究进展加以综述。

【关键词】 卵巢储备功能减退; 原发卵巢功能不足; 脆性 X 智力低下基因突变

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Study on the molecular mechanism of fragile X-associated primary ovarian insufficiency and diminished ovarian reserve

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【Abstract】 Fragile X mental retardation 1 (FMR1) has been shown to be the most significant single gene associated with primary ovarian insufficiency (POI) and diminished ovarian reserve (DOR). *FMR1* gene mutant can lead to fragile X-associated primary ovarian insufficiency (FXPOI) and fragile X-associated diminished ovarian reserve (FXDOR). However, the molecular mechanisms that compromise follicular function are unknown. It was suggested that toxic *FMR1* mRNA gain of function, fragile X mental retardation protein (FMRP) acting as translational repressors, FMRpolyG in ubiquitin-positive inclusions, histone modification pattern in regulation of *FMR1* gene and down-regulated transcription profiling could be involved in FXPOI and FXDOR. We reviewed that the research progress on the molecular mechanism of ovarian dysfunction caused by *FMR1* gene.

【Key words】 Diminished ovarian reserve; Primary ovarian insufficiency; Fragile X mental retardation 1 gene mutation

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