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低分子肝素防治自然流产中国专家共识

低分子肝素防治自然流产中国专家共识编写组

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【摘要】 低分子肝素 (LMWH) 是一类高效、相对安全的糖类抗凝剂。为了进一步指导和规范 LMWH 在自然流产防治中的应用, 妇产科学、生殖医学、风湿免疫病学以及药理学等领域的相关专家根据国内外的研究进展, 结合我国的实际情况, 针对 LMWH 防治自然流产的适应证、剂量、疗程、监测等方面进行了充分讨论, 并制定了该共识。共识指出 LMWH 用于防治自然流产的适应证主要是抗磷脂综合征 (APS)、易栓症 (PTS)、自身免疫性疾病 (AID) 等。依据病情, LMWH 使用剂量有预防剂量和治疗剂量。对于不明原因的反复自然流产 (URSA)、反复生化妊娠 (RBP) 和反复种植失败 (RPF) 患者使用 LMWH 能否改善妊娠结局尚缺乏依据, 尚无足够的临床证据显示增加 LMWH 剂量能增加血 β - 人绒毛膜促性腺激素 (hCG) 水平。对于合并高血压、糖尿病、慢性肾脏疾病等病程较长、有可能存在血管内皮损伤的反复自然流产 (RSA) 患者, 可以适当应用 LMWH, 但疗效有待进一步临床验证。临床上应避免超适应证和超大剂量使用。

【关键词】 低分子肝素 (LMWH); 自然流产; 防治; 共识

· 标准与规范 ·

Chinese experts consensus on prevention and treatment of spontaneous abortion with low molecular weight heparin

Chinese Experts Consensus Group on Low Molecular Weight Heparin for Prevention and Treatment of Spontaneous Abortion, China

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【Abstract】 Low molecular weight heparin (LMWH) is a kind of high efficiency and relatively safety sugar anticoagulants. To further guide and standardize the application of LMWH in the prevention and treatment of natural abortion, this consensus, including the indications, dosage, treatment course, and monitoring of natural abortion in LMWH, was made by experts in the fields of obstetrics and gynecology, reproductive medicine, rheumatology and pharmacology. The consensus points out that the indications of LMWH for the prevention and treatment of natural abortion are mainly antiphospholipid syndrome (APS), pre-thrombotic state (PTS), autoimmune disease (AID), etc. According to the condition, LMWH can be used with preventive dosage and therapeutic dosage. Whether LMWH can improve pregnancy outcome in patients with unexplained recurrent spontaneous abortion (URSA), repeated biochemical pregnancy (RBP), and repeated planting failure (RPF) is unproven, and there is no enough clinical evidence to show that LMWH can increase the level of blood β -human chorionic gonadotrophin (hCG). LMWH can be applied to patients with recurrent spontaneous abortion (RSA) who also have a long course of hypertension, diabetes, chronic kidney diseases and may have vascular endothelial injury, but the efficacy remains to be further verified. Clinically, indications range expansion and super-large dosage should be avoided.

【Key words】 Low molecular weight heparins (LMWH); Spontaneous abortion; Prevention and treatment; Consensus

· 生育力保存 ·

玻璃化冷冻和程序化冷冻方法对人类卵母细胞骨架及其发育潜能的影响

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【摘要】目的 探讨玻璃化冷冻和程序化冷冻对人卵母细胞纺锤体定位、细胞骨架及其发育潜能的影响。**方法** 将第2日发育为M_{II}卵母细胞随机分为对照组、程序化冻融组、玻璃化冻融组(解冻0 h、1 h、3 h)。应用液晶偏振光显微镜(Polscope)成像系统观察卵母细胞纺锤体与第一极体(Pb)的夹角、表面积、卵透明带内层光阻值和外层光阻值。采用扫描电子显微镜和透射电子显微镜观察卵母细胞的表面和内部超微结构。统计2种冻融方法对卵母细胞发育潜能的影响。**结果** 对照组、程序化冷冻解冻培养3 h组和玻璃化冷冻解冻后培养0 h、1 h、3 h组中的纺锤体可见率分别为92.4%、56.4%、11.2%、24.8%、61.1%。与程序化冻融组相比,玻璃化冷冻解冻培养3 h后卵母细胞中纺锤体与Pb的夹角更小(37.3°与68°, $P=0.023$)。对照组、程序化冻融组和玻璃化冻融后培养3 h组中卵母细胞的纺锤体面积、卵透明带内层光阻值和透明带外层光阻值差异无统计学意义($P>0.05$)。与程序化冻融组相比,玻璃化冻融后培养3 h组中卵母细胞表面突起丰富,微绒毛形态较为正常,倒伏在细胞表面,卵透明带边界较为清晰,与对照组较为接近。程序化冻融组的正常受精率(65.7%)明显低于对照组(79.2%, $P=0.041$),而卵裂率和囊胚形成率与对照组和玻璃化冻融组差异无统计学意义($P>0.05$)。玻璃化冻融后培养3 h组中正常受精率、卵裂率、囊胚形成率与对照组相比,差异无统计学意义($P>0.05$)。**结论** 相比程序化冷冻,玻璃化冷冻对卵母细胞纺锤体和卵透明带的损伤及对卵母细胞的发育潜能的影响都较小,可以作为卵母细胞冷冻的一种有效方法。

【关键词】 玻璃化冷冻; 程序化冷冻; 人类卵母细胞; 纺锤体; 卵透明带

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· 生育力保存 ·

Effects of vitrification and slow freezing on ultrastructure and developmental potential of human oocytes

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【Abstract】 Objective To compare the the spindles, cytoskeleton and the developmental potential of human oocytes between vitrification and slow freezing approaches by polscope and electron microscopy.

Methods The immature human oocytes were randomly divided into control, slow freezing, and vitrification freezing-thawing groups (0 h, 1 h, 3 h after thawing). The spindle, the angle of spindle to the first polarbody, the surface area of oocytes and the lining and outer retardance of zona pellucida were observed by Polscope. The surface and ultrastructure of oocytes were observed by scanning electron microscopy (SEM) and transmission electron microscopy (TEM). Finally, the influences of two freezing methods on developmental capability of human oocytes were analyzed.

Results The visible rate of spindle was 92.4%, 56.4%, 11.2%, 24.8%, 61.1% in control group, slow freezing-thawing group, and vitrification freezing-thawing after 0 h, 1 h and 3 h, respectively. Compared with slow freezing, the angle of the spindle to the first polar body in vitrification freezing-thawing after 3 h group was smaller (37.3° , 68° , $P=0.023$). No significant differences were observed in the surface area of oocytes, the lining and outer ret of oocytes zona pellucida between vitrification freezing-thawing after 3 h group and slow freezing group. The protrusions of oocyte surface were increased, the microvilli were normal, and laid down on the membrane surface in vitrification freezing-thawing after 3 h group than slow freezing group, and similar results of better recovery of perivitelline space and mitochondria were obtained. The 2 pronucleus (PN) fertilization rate in slow freezing group (65.7%) was decreased compared with control group (79.2%, $P=0.041$). No significant differences were observed between vitrification freezing-thawing after 3 h group and control group in 2PN fertilization rate, cleavage rate and blastocyst formation rate.

Conclusion Preliminary results suggest that the vitrification freezing-thawing for oocyte cryopreservation is a better choice than slow freezing-thawing.

【Key words】 Vitrification; Slow freezing; Human oocyte; Meiotic spindle; Oocyte zona pellucida

Fund program: National Nature Science Foundation of China (Youth Project, 81701419); National Nature Science Foundation of China (81571418)

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新型超微量冷冻麦管：微量精子冻融安全有效新载体（附 83 例报道）

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【摘要】 目的 探讨新型超微量冷冻麦管 (LSL 管) 冻存微量精子的冻融结果。方法 回顾性分析 83 例严重男性不育症患者采用 LSL 管冻存精子的冻融结果，观察其中 23 对夫妇因男性因素解冻 LSL 管精子行卵胞质内单精子显微注射 (intracytoplasmic sperm injection, ICSI) 的妊娠结局。结果 不同来源的微量精子采用 LSL 管复苏后 89.5%(94/105) 可见活动精子，进入辅助生殖周期的标本可使用率为 73.9%(17/23)。在 18 个 ICSI 周期中，受精率、卵裂率、可用胚胎率和优质胚胎率分别为 78.0%、92.5%、62.7% 和 40.6%；种植率、临床妊娠率和累计活产率分别为 31.1%、52.5% 和 55.6%。获得的所有 12 个活产儿均未见出生缺陷。结论 LSL 管是一种可用于微量精子冷冻保存的安全有效新载体，可广泛使用于辅助生殖治疗。

【关键词】 微量精子；冻融；新型超微量冷冻麦管 (LSL 管)；卵胞质内单精子显微注射 (ICSI)；妊娠结局

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A novel micro-straw (LSL straw): the reliable cryopreservation vehicle for rare or very low concentrations of human sperm (83 cases reported)*Xue Yunjing, Xu Yuan, Liu Feng, Zhu Zijue, Gong Yuehua,**Wang Xiaobo, Hu Jianlin, Sun Jian, Chen Wei, Zhang Zhenbo, Wu Yu, Li Zheng**Department of Andrology, Center for Men's Health, Department of ART, Institute of Urology, Urologic Medical Center, Shanghai General Hospital, Shanghai Key Lab of Reproductive Medicine, Shanghai Jiao Tong University, Shanghai 200080, China (Xue YJ, Xu Y, Liu F, Zhu ZJ, Gong YH, Wang XB, Hu JL, Sun J, Chen W, Zhang ZB, Wu Y, Li Z)**Corresponding author: Wu Yu, Tel: +86-13761290479, Email: yuwu818@163.com;**Li Zheng, Tel: +86-13564783816, Email: lizhengboshi@163.com**Xue Yunjing and Xu Yuan are the first authors who contributed equally to the article*

【Abstract】 Objective To analyze the pregnancy outcome of cases who underwent intracytoplasmic sperm injection (ICSI) with frozen-thawed sperm, which was rare and weak, cryopreserved by a novel micro-straw (LSL micro-straw). **Methods** The present study retrospectively analyzed the post-thaw results of cryopreserved human sperm from 83 severe infertility male patients (including oligospermia and asthenospermia). Then we investigated the evolution of embryo development and pregnancy outcome in 23 patients underwent ICSI. **Results** About 89.5% (94/105) frozen-thawed samples could observe motile sperm in quality control. About 73.9% (17/23) sperm were available in 18 ICSI cycles. The fertilization rate, the cleavage rate, the available embryo rate and the high-quality embryo rate were 78.0%, 92.5%, 62.7% and 78.0%, respectively. The implantation rate, the clinical pregnancy rate and the cumulative live birth rate were 31.1%, 52.5% and 55.6%, respectively. Totally 12 live births were obtained with no birth defects reported. **Conclusion** LSL micro-straw is a safe and feasible new carrier for cryopreservation of oligospermia and asthenospermia, which can be widely applied in assisted reproductive technology.

【Key words】 Rare human spermatozoa; Freezing and thawing; Novel micro-straw (LSL micro-straw); Intracytoplasmic sperm injection (ICSI); Pregnancy outcomes

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· 生育力保存 ·

冻存卵巢组织移植成功——首次报道

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【摘要】目的 通过卵巢组织冻存技术及自体移植手术保护癌症患者生育力与内分泌功能。**方法** 对 1 例 40 岁宫颈鳞癌 IIb 期患者在放化疗前进行卵巢组织取材、冻存, 待其癌症痊愈后进行冻存卵巢组织自体移植手术, 随访监测患者的激素水平、卵泡发育情况、月经恢复情况以及绝经相关症状。**结果** 卵巢组织移植 4 个月后, 改良 Kupperman 评分由 20 分降低至 <5 分, 绝经相关症状基本消失, 卵泡刺激素 (FSH) 降低至 22.79 IU/L, 此后继续下降至 6 IU/L, 雌二醇 (E₂) 由 <11.8 ng/L 升高至 84.46 ng/L, B 超监测到有卵泡发育且月经恢复。**结论** 卵巢组织冻存移植 4 个月后卵巢功能恢复正常, 证明卵巢组织在临床上移植成功。

【关键词】 卵巢组织冻存; 移植; 宫颈癌; 卵巢储备功能

基金项目: 北京市医院管理局临床医学发展专项经费资助 (XMLX201710); 首都卫生发展科研专项 (首发 2016-2-2113); 首都临床特色应用研究课题 (Z161100000516143); 北京市医院管理局“登峰”计划专项经费资助 (DFL20181401); 北京市卫生系统高层次卫生技术人才 (2014-2-016); 2018 年度国家外专局引智重点项目 (20181100005); 中国国际人才交流促进会医疗健康技术创新与人才培养专项基金 (2017041900004, 2018042000001)

· 生育力保存 ·

Successful auto-transplantation of frozen-thawed ovarian tissue reported for the first time

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【Abstract】 Objective To preserve fertility and endocrine function of a cervical cancer patient by ovarian tissue cryopreservation and auto-transplantation. **Methods** Part of ovary was harvested and cryopreserved before chemo- and radio-therapy for a 40-year-old woman who was diagnosed with cervical squamous carcinoma. After the cervical cancer reached to remission, the patient underwent cryopreserved ovarian tissue transplantation. The endocrine hormone, follicle growth, restoration of menstruation and menopausal syndromes were detected. **Results** Four months after the surgery of transplantation, the modified Kupperman scores decreased from 20 to less than 5, and the menopausal syndrome disappeared. The concentration of follicle-stimulating hormone (FSH) decreased to 22.79 IU/L and then decline to 6 IU/L, the concentration of estradiol (E₂) increased from <11.8 ng/L to 84.46 ng/L. Follicle growth was observed by ultrasound and the menstruation has been restored. **Conclusion** After the transplantation of cryopreserved ovarian tissue, the ovarian function has returned to normal, which demonstrated the success of transplantation of frozen-thawed ovarian tissue.

【Key words】 Ovarian tissue cryopreservation; Transplantation; Cervical cancer; Ovarian reserve function

Fund program: Beijing Municipal Administration of Hospitals Clinical Medicine Development of Special Funding Support (XMLX201710); Capital's Funds for Health Improvement and Research (2016-2-2113); Beijing Municipal Science & Technology Commission (Z161100000516143); Beijing Municipal Administration of Hospitals' Ascent Plan (DFL20181401); Beijing Municipality Health Technology High-level Talent (2014-2-016); SAFEA: Project for Key Foreign Experts in 2018 (20181100005); China International Talent Exchange Association, Medical Health Technology Innovation and Talent Training Special Fund (2017041900004,

·生育力保存·

非梗阻性无精子症患者采用睾丸显微取精术联合睾丸组织混悬液冷冻的临床效果

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【摘要】 目的 探讨睾丸显微取精术 (micro-TESE) 联合睾丸组织混悬液冷冻治疗不同病理类型的非梗阻性无精子症 (non-obstructive azoospermia, NOA) 行卵胞质内单精子显微注射 (intracytoplasmic sperm injection, ICSI) 的临床结局。方法 回顾性分析 2016 年 3 月—2017 年 3 月期间本中心经 Micro-TESE 手术获取精子并进行睾丸组织混悬液冷冻的 NOA 患者的 ICSI 结局。结果 70 例 NOA 患者中, micro-TESE 获得精子 30 例 (42.9%)。睾丸生精细胞成熟阻滞者 (maturation arrest, MA) 的获精率 (sperm retrieval rate, SRR) 显著低于生精功能低下者 (hypo-spermatogenesis, H-S), 差异有统计学意义 ($P=0.00$), 但同唯支持细胞综合征 (Sertoli cell only syndrome, SCOS) 比较, 差异无统计学意义 ($P=0.64$)。而早期睾丸生精细胞成熟阻滞 (early MA) 的 SRR[20.8%(5/24)] 低于晚期生精细胞成熟阻滞 (late MA) [43.8%(7/16)]。30 例睾丸组织混悬液解冻行 ICSI 注射, 临床妊娠率为 46.7%(14/30)。其中, MA 组临床妊娠率为 41.7%(5/12); H-S 组临床妊娠率为 47.1%(8/17); SCOS 组 1 例行 ICSI 后临床妊娠。结论 在辅助生殖技术中, 睾丸显微取精术联合睾丸组织混悬液冷冻治疗 NOA 患者, 临床结果满意。

【关键词】 睾丸显微取精术 (micro-TESE); 睾丸组织混悬液冷冻; 非梗阻性无精子症 (NOA); 卵胞质内单精子注射 (ICSI)

基金项目: 国家自然科学基金青年项目资助 (81401191)

·生育力保存·

Clinical evaluation of micro-testicular sperm extraction combined with testicular tissue suspensions cryopreservation in the treatment of non-obstructive azoospermia *An Geng, Fu Xin, Kang Xiangjin,*

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【Abstract】 Objective To investigate the intracytoplasmic sperm injection (ICSI) outcome of testicular tissue suspensions cryopreservation combined with micro-testicular sperm extraction (TESE) in the treatment of non-obstructive azoospermia (NOA) with different pathological types. **Methods** We retrospectively analyzed the ICSI outcome of NOA patients undergoing micro-TESE and testicular tissue suspensions cryopreservation from March 2016 to March 2017. **Results** In 70 cases of NOA, spermatozoa of 30 cases (42.9%) were obtained from micro-TESE. The sperm retrieval rate (SRR) of the patients with spermatogenic cells maturation arrest was significantly lower than that of the patients with hypo-spermatogenesis (H-S) ($P=0.00$). However, compared with Sertoli cell only syndrome (SCOS), the difference was not statistically significant ($P=0.64$). The SRR of early maturation arrest [20.8% (5/24)] was lower than that of late maturation arrest [43.8% (7/16)]. Thirty cases of testicular tissue thawed were injected with ICSI. The clinical pregnancy rate was 46.7%. The clinical pregnancy rate was 41.7% in maturation arrest group and 47.1% in H-S group. **Conclusion** In the assisted reproductive technique, the clinical results testicular of tissue suspensions freezing combined with micro-TESE for NOA patients are satisfactory, which would provide new ideas and options for clinical treatment of NOA patients.

【Key words】 Micro-testicular sperm extraction (TESE); Testicular tissue suspensions freezing; Non-obstructive azoospermia (NOA); Intracytoplasmic sperm injection (ICSI)

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·生育力保存·

女性肿瘤患者生育力保存 39 例报告

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【摘要】目的 探讨女性肿瘤患者的疾病分类与生育力保存方案的效率。**方法** 本研究回顾性分析本院生殖中心生育力保存库患者的基本情况, 以及生育力保存的方式和效果。**结果** 进行生育力保存的 39 例女性患者, 年龄 13~39 岁, 以乳腺癌和非霍奇金淋巴瘤为主要病种, 其中 10 例行胚胎冷冻, 平均冻存胚胎 5 个, 14 例冷冻卵子, 平均冻存卵子 9 个, 15 例冷冻卵巢组织, 平均冻存卵巢组织 14 片。**结论** 40 岁以下女性肿瘤患者, 可探索进行放化疗前生育力保存。

【关键词】 女性; 肿瘤; 生育力保存

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· 生育力保存 ·

Fertility preservation in female tumor patients: a report of 39 cases *Li Tingting, Guo Yingchun, Li Qian,*

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【Abstract】 Objective To analyse female fertility preservation situation who were diagnosed with cancer.

Methods This study retrospectively analyzed the female fertility preservation situation of tumor patients in the Reproductive Center of Sixth Affiliated Hospital, Sun Yat-sen University. As well as explore the ways and effects of female fertility preservation. **Results** There were 39 female cancer patients, age from 13 to 39 years old. Breast cancer and lymphoma were main diseases to them. Among them, 10 patients choosed frozen embryos with an average of 5 embryos frozen, and 14 patients choosed frozen eggs with an average of 9 eggs frozen, 15 patients choosed frozen ovarian tissue with an average of 14 ovarian slices frozen. **Conclusion** Fertility preservation is an effective method for female cancer patients under the age of 40 years before chemoradiotherapy.

【Key words】 Female; Neoplasms; Fertility preservation

Fund program: Guangdong Medical Science and Technology Research Fund (A2015025); The Prevention and Control Research of Reproductive Health and Main Birth Defects, National Key R&D Program of China (2016YFC1000302)

· 生育力保存 ·

化疗药物对卵巢功能的损伤机制及生育力保护

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【摘要】 化疗在治疗恶性肿瘤的同时可造成卵巢功能的损伤, 引起闭经和不孕。对不同的化疗药物损伤机制的了解, 可使我们有针对性地实现生育力的保护。已证实有多种方法及药物可保护卵巢功能, 实现生育力的保护。本文将对化疗药物对卵巢功能的损伤机制及生育力保护的相关进展作一综述。

【关键词】 化疗; 卵巢功能; 生育力保护

· 生育力保存 ·

Mechanisms of chemotherapy-induced ovarian damage and fertility preservation Fu Zijie, Li Xiaodong

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【Abstract】 Chemotherapy can induce ovarian damage while treating malignant tumor, which causes amenorrhea and infertility. The understanding of the mechanisms of chemotherapy-induced ovarian damage may lead to targeted treatments to preserve fertility. It has been proved that there are many methods and medicines to protect ovarian function and realize the preservation of fertility. This article reviews the mechanisms of chemotherapy-induced ovarian damage and the progress of fertility preservation.

【Key words】 Chemotherapy; Ovarian function; Fertility preservation

· 临床研究 ·

不孕症合并子宫内膜非典型增生及早期高分化子宫内膜样腺癌保守治疗后体外受精助孕的临床分析

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【摘要】 目的 探讨不孕症合并子宫内膜非典型增生 (AEH) 及早期高分化子宫内膜样腺癌 (EC) 药物保守治疗后体外受精 (IVF) 助孕时机、疗效及安全性。方法 回顾性分析本中心不孕症合并 AEH 及 EC 保守治疗后行 IVF 助孕患者的临床资料, 根据患者首次子宫内膜病理证实病变完全消退 (CR) 后开始 IVF 助孕时间分为 ≤ 3 个月组 (A 组, $n=35$) 和 >3 个月组 (B 组, $n=25$), 比较组间患者的临床结局。结果 共纳入 60 例患者, AEH 患者 45 例, EC 患者 15 例, 首次 CR 后随访时间 (39.6 ± 26.9) 个月。共行 95 个取卵周期, 新鲜胚胎移植 (IVF-ET) 67 个周期, 周期妊娠率为 38.8% (26/67), 冻融胚胎移植 (FET) 54 个周期, 周期妊娠率为 25.9% (14/54)。共有 36 例患者妊娠 47 次, 25 例患者分娩 32 个活婴。患者 IVF-ET 周期妊娠率及 FET 周期妊娠率组间比较差异均无统计学意义, 而 B 组复发率 (48.0%) 明显高于 A 组 (17.1%, $P=0.022$)。多因素分析显示仅 IVF 助孕时间与复发有关 ($P=0.002$, $OR=1.078$, 95% $CI=1.027 \sim 1.132$)。随访期间总复发率为 30.0% (18/60), 无疾病进展及死亡不良事件。结论 不孕症合并 AEH 及早期 EC 患者药物保守治疗后 IVF 助孕是相对安全有效的, 复发与首次 CR 后 IVF 助孕时间有关, 为降低复发宜尽早行 IVF 助孕。

【关键词】 不孕症; 子宫内膜; 非典型增生 (AEH); 子宫内膜癌; 体外受精 (IVF)

· 临床研究 ·

Analysis of the clinical outcome of *in vitro* fertilization in infertility patients with conservative treatment of atypical endometrial hyperplasia and early well-differentiated endometrial adenocarcinoma Du Xiaoguo,

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【Abstract】 Objective To investigate the timing, efficacy and safety of *in vitro* fertilization (IVF) in infertility patients with conservative treatment of atypical endometrium hyperplasia (AEH) and early well-differentiated endometrial adenocarcinoma (EC). **Methods** The clinical data of infertility patients with conservative treatment of AEH and early high differentiation EC, who underwent IVF treatment were retrospectively analyzed according to the time to start IVF after endometrial pathology confirmed that the lesion completely response (CR), the patients were divided into ≤ 3 months (group A, $n=35$) and > 3 months (group B, $n=25$). The clinical outcomes of the two groups were compared. **Results** A total of 60 patients were included, 45 with AEH and 15 with EC. The follow-up time from the first time to achieve CR was (39.6 ± 26.9) months. Totally 95 IVF cycles were performed, including 67 fresh embryo transfer cycles, the rate of pregnancy per cycle was 38.8% (26/67), and 54 frozen-thawed embryo transfer (FET) cycles, the rate of pregnancy per cycle was 25.9% (14/54). A total of 36 patients were pregnant 47 times, 25 patients delivered 32 live births. There were no statistical differences in the IVF-ET cycle pregnancy rate and FET cycle pregnancy rate between the two groups, and the recurrence rate was significantly higher in group B (48.0%) than in group A (17.1%, $P=0.022$), with a statistical significance. Multifactorial analysis showed that only the time of IVF treatment after the first CR was related to recurrence ($P=0.002$, $OR=1.078$, 95% $CI=1.027-1.132$). The total recurrence rate was 30.0% (18/60) during the follow-up period, with no disease progression and adverse events. **Conclusion** Infertility patients with conservative treatment of AEH and early well-differentiated EC undergoing IVF treatment is relatively safe and effective. Recurrence is associated with the time of IVF treatment after the first time to achieve complete response, in order to reduce recurrence, IVF should be used as soon as possible.

【Key words】 Infertility; Endometrium; Atypical hyperplasia; Endometrial adenocarcinoma; *In vitro* fertilization (IVF)

· 实验研究 ·

间质 - 上皮转化参与子宫内膜异位症模型大鼠包囊形成

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【摘要】 目的 探讨间质上皮转化以及转录因子 Snail 在子宫内膜异位症 (EMS) 模型大鼠异位包囊形成中的作用。方法 自体移植法建立 EMS 大鼠模型。选取造模成功形成包囊的 EMS 大鼠, 分为造模后 2 周至 7 周组, 取正常大鼠为正常对照组。采用免疫组织化学方法研究上皮标志物 (E- 钙黏蛋白、角蛋白 8)、间质标志物 (波形蛋白) 以及 Snail 在异位内膜包囊中的定位和表达情况, Western blotting 法检测 E- 钙黏蛋白、波形蛋白在异位内膜包囊形成组织中的含量。采用 TUNEL 法检测异位包囊内部脱落细胞凋亡情况。**结果** 免疫组织化学结果显示, EMS 模型大鼠的异位内膜包囊腔上皮 E- 钙黏蛋白、角蛋白 8 和波形蛋白含量在造模后 2~7 周过程中, 相对于包囊壁间质层均处于较高水平, 而且与正常子宫内膜上皮比较, 亦处于较高的水平。另发现造模后 2~7 周异位包囊腔上皮样细胞脱落, E- 钙黏蛋白、角蛋白 8、波形蛋白阳性表达, 且在造模后 4~5 周阳性信号最强。与正常大鼠子宫内膜组织比较, 造模后 3~5 周异位内膜包囊腔上皮中 Snail 阳性表达信号增强。Western blotting 法检测显示, 造模后 2~7 周异位内膜中 E- 钙黏蛋白、波形蛋白含量与正常内膜比较, 均维持在较高水平, 差异均有统计学意义 ($P < 0.05$)。TUNEL 法检测发现异位包囊内部脱落细胞未发生凋亡。**结论** EMS 模型大鼠异位包囊腔上皮细胞可能是由间质细胞转化形成, 提示间质 - 上皮转化 (MET) 参与了异位包囊形成, 且 Snail 参与调控其过程; 异位内膜包囊上皮细胞脱落以形成囊腔, 但其上皮细胞脱落不伴随细胞凋亡。

【关键词】 子宫内膜异位症 (EMS); 大鼠; 自体移植模型; 间质 - 上皮转化 (MET); 包囊发生

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· 实验研究 ·

Mesenchymal epithelial transformation is involved in the formation of cysts in endometriosis rats

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【Abstract】 Objective To investigate the role of stromal epithelial transformation and Snail in ectopic cyst formation in endometriosis (EMS) rats. **Methods** The model of EMS rats was established by autologous transplantation. EMS rats were successfully divided into 2-7 weeks after modeling. The normal rats were taken as the normal control group. Immunohistochemical method was used to study the localization and expression of epithelial marker (E-cadherin, cytokeratin 8), mesenchymal marker (vimentin) and Snail in ectopic endometrial cysts. Western blotting was performed to detect the expression of E-cadherin and vimentin in endometriotic cyst. TUNEL method was used to detect the apoptosis of exfoliated cells in ectopic cyst. **Results** Immunohistochemistry showed that the EMS rat model of endometriotic cyst cavity epithelial E-cadherin, cytokeratin 8 and vimentin in the model after 2-7 weeks in the process, relative to the cyst wall stroma are at a high level, but compared with the normal endometrial epithelium, also at a higher level. In addition, 2-7 weeks ectopic cyst epithelial cell shedding, positive expression of E-cadherin, cytokeratin 8 and vimentin, and 4-5 weeks after modeling, the positive signal was the strongest. Compared with normal rat endometrial tissue, Snail positive expression signal was enhanced in the ectopic endometrium cyst cavity epithelium 3-5 weeks after modeling. The Western blotting result showed that the content of E-cadherin and vimentin in the ectopic endometrium after 2-7 weeks was significantly higher than that in the normal endometrium, and the difference was statistically significant ($P < 0.05$). TUNEL assay showed no apoptosis in the exfoliated cells of ectopic cysts. **Conclusions** The epithelial cells in ectopic cystic cavity of EMS model rats may be formed by the transformation of mesenchymal cells, suggesting that the mesenchymal epithelial transformation is involved in the formation of ectopic cysts, Snail regulates MET development, and epithelial cells in the ectopic endometrium cyst cavity are detached. The formation of a cavity constitutes an ectopic endometrial cyst of an EMS model rat, and epithelial cells shedding to form a cyst without involvement of apoptosis.

【Key words】 Endometriosis (EMS); Rats; Autologous transplantation models; Stromal epithelial transformation; Cysts

Fund program: The National Nature Science Foundation of China (General Program) (81373684); Shanghai

· 实验研究 ·

康妇炎胶囊调节衣原体感染的中性粒细胞的活性

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【摘要】目的 观察康妇炎胶囊对衣原体感染的中性粒细胞 (PMN) 活性的影响, 研究其杀菌消炎机理。方法 分离大鼠外周血 PMN, 衣原体感染 6 h 后予以 10 ng/mL (K-10 ng 组)、10 μ g/mL (K-10 μ g 组)、1 mg/mL (K-1 mg 组) 康妇炎胶囊处理 6 h、12 h、24 h 后, 分别收集培养液和细胞分析活性氧簇 (ROS)、髓过氧化物酶 (MPO) 和衣原体载量。利用 TLR2/4 激动剂或抑制剂, 分析康妇炎胶囊影响 PMN 活性的分子机理。结果 康妇炎处理衣原体感染的 PMN 后, 显著降低细胞内 ROS (K-1 mg: 6 h $P=0.000\ 03$ 、12 h $P=0.000\ 001$ 、24 h $P=0.000\ 003$; K-10 μ g: 6 h $P=0.014$ 、12 h $P=0.009$ 、24 h $P=0.009$; K-10 ng: 24 h $P=0.000\ 5$) 和 MPO (K-1 mg: 6 h $P=0.046$ 、12 h $P=0.004$ 、24 h $P=0.038$; K-10 μ g: 12 h $P=0.048$ 、24 h $P=0.011$; K-10 ng: 12 h $P=0.005$ 、24 h $P=0.017$) 水平, 显著降低培养液中衣原体载量 (K-10 ng: $P=0.000\ 2$; K-10 μ g: $P=0.000\ 1$; K-1 mg: $P=0.002$)。相比于康妇炎组, TLR4 抗体与康妇炎同时作用于细胞, 显著抑制 PMN 分泌 MPO ($P=0.011$); TLR2 和 TLR4 激动剂分别与康妇炎作用细胞, 培养液中衣原体负荷量显著降低 (PGN: $P=0.002$; LPS: $P=0.000\ 08$)。结论 康妇炎胶囊通过抑制 PMN 产生和分泌 ROS 和 MPO, 促进 PMN 吞噬衣原体, 调节 PMN 的杀菌方式, 减少脱颗粒物如 ROS、MPO 的产生, 促进对病原菌的吞噬, 减少因 PMN 脱颗粒释放 ROS 和 MPO 到细胞外引起组织损伤, 但其调节 PMN 杀菌方式的分子机理与 TLR2/4 信号通路不重叠。

【关键词】中性粒细胞; 康妇炎胶囊; 活性氧簇 (ROS); 髓过氧化物酶 (MPO); 吞噬

· 实验研究 ·

Activity of neutrophils infected by *Chlamydia trachomatis* is modulated by Kang Fuyan capsule Li Shanshan, Zhou Yuanping, Xie Zhenwei, Xu Jian

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【Abstract】 Objective To explore the effects and mechanisms of Kang Fuyan capsule for the treatment of inflammation through observing the activity of polymorphonuclear neutrophils (PMN) infected by *Chlamydia trachomatis* (CT). **Methods** Rat peripheral blood PMN was separated and cultured. After infecting CT for 6 h, PMN was treated with Kang Fuyan capsule [10 ng/mL (K-10 ng group), 10 μg/mL (K-10 μg group), 1 mg/mL (K-1 mg group)] for 6 h, 12 h and 24 h. Cells and cell supernatant were collected to analyze reactive oxygen species (ROS), myeloperoxidase (MPO) and CT loads. Molecular mechanisms of Kang Fuyan capsule affecting the activity of PMN in inflammatory response caused by CT were researched by TLR2/4 agonist or inhibitors. **Results** PMN intracellular ROS level was increased significantly ($P < 0.001$) after CT infecting PMN. Kang Fuyan capsule significantly inhibited the production of ROS (K-1 mg: 6 h $P = 0.000\ 03$, 12 h $P = 0.000\ 001$, 24 h $P = 0.000\ 003$; K-10 μg: 6 h $P = 0.014$, 12 h $P = 0.009$, 24 h $P = 0.009$; K-10 ng: 24 h $P = 0.000\ 5$) and MPO (K-1 mg: 6 h $P = 0.046$, 12 h $P = 0.004$, 24 h $P = 0.038$; K-10 μg: 12 h $P = 0.048$, 24 h $P = 0.011$; K-10 ng: 12 h $P = 0.005$, 24 h $P = 0.017$) and inhibited the CT load of cell culture medium. Compared with Kang Fuyan capsule group, TLR4 inhibitors and Kang Fuyan capsule acting on cells at the same time significantly inhibit the secretion of MPO ($P = 0.011$); TLR2/4 agonist and Kang Fuyan capsule acting on cells at the same time significantly decreased the CT load in cell supernatant (PGN: $P = 0.002$; LPS: $P = 0.000\ 08$). **Conclusion** Kang Fuyan capsule regulates the sterilization ways of PMN by suppressing the production and secretion of ROS and MPO, and promoting PMN phagocytosis. But the molecular mechanisms of Kang Fuyan capsule to PMN had nothing to do with TLR2/4 and still need to be studied.

【Key words】 Polymorphonuclear neutrophils; Kang Fuyan capsule; Reactive oxygen species (ROS); Myeloperoxidase (MPO); Phagocytosis

· 综述 ·

环状 RNAs 的生物学功能及其与胚胎发育和复发性流产的关系

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【摘要】 环状 RNAs(circular RNAs, circRNAs) 是一类呈共价闭环状结构的新型竞争性内源性非编码 RNAs 分子, 广泛存在于真核细胞质中, 具有调控基因表达的重要生物学功能。鉴于 circRNAs 在不同疾病中承担着特定的调控角色, 有成为疾病诊断和治疗的新型生物标志物的巨大潜力, 本文概述了 circRNAs 的生物学功能, circRNAs 与胚胎发育和复发性流产 (recurrent spontaneous abortion, RSA) 的关系及其研究前景。

【关键词】 环状 RNAs(circRNAs); 生物学功能; 胚胎发育; 复发性流产

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· 综 述 ·

Biological functions of circular RNAs and relationships of circRNA with embryonic development and recurrent spontaneous abortion *Liu Junwei, Zhang Zhaofeng, Xu Jianhua, Pi Li, Du Jing*

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【Abstract】 Circular RNAs (circRNAs) are a new class of competing endogenous non-coding RNA molecule with a covalently closed loop structure. CircRNAs are abundant in the eukaryotic cell cytoplasm and have many important biological functions in the regulation of gene expression. Given its specific regulatory roles in diverse diseases, circRNAs have significant potential to become new clinical diagnostic biomarkers and targets for treatment. In this article, we summarize the biological functions of circRNAs, the relationships of circRNAs with embryonic development and recurrent spontaneous abortion (RSA) and discussed its research prospects.

【Key words】 Circular RNAs (circRNAs); Biological functions; Embryonic development; Recurrent spontaneous abortion (RSA)

Fund program: National Natural Science Foundation of China (81571503, 81771655); Innovation-oriented Science and Technology Grant from NPFPC Key Laboratory of Reproduction Regulation (CX2017-03)

· 综 述 ·

抗磷脂综合征分类标准外的临床表现及抗体研究进展

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【摘要】 2006 年悉尼分类标准是目前诊断抗磷脂综合征 (antiphospholipid syndrome, APS) 公认的标准, 它提高了 APS 诊断的特异性, 但在一定程度上降低了敏感性。标准外的临床表现与抗磷脂抗体及血栓的风险相关, 充分认识它们能够影响治疗决策, 改善部分血清学检查提示 APS 但临床症状不满足即 APS 可能 (probable APS) 患者的预后。此外, 随着研究的进展, 越来越多新的抗体等标志物被发现与血栓事件和不良妊娠事件相关, 这些新的抗体可以帮助血清阴性 APS (seronegative APS, SNAPS) 患者, 即临床症状符合疾病表现但实验室检查阴性进行风险评估, 同时为制定治疗决策提供依据。本文将围绕 APS 分类标准以外的临床表现和抗体的研究进展作一综述。

【关键词】 抗磷脂综合征 (APS); 标准外的临床表现; 非传统抗磷脂抗体; 血清阴性抗磷脂综合征 (SNAPS)

· 综 述 ·

Research advances on ‘extra-criteria’ manifestations and antibodies in antiphospholipid syndrome Gu Jieyu,

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【Abstract】 The 2006 Sydney classification criteria, which is most commonly used in the diagnosis of antiphospholipid syndrome (APS) by far, improves the sensitivity of the diagnosis but suffers a lack of specificity. Extra-criteria manifestations are associated with antiphospholipid antibody (aPL) and thrombosis, thus fully recognizing them could help make treatment decision and improve the prognosis of part of the patients with probable APS, in whom serological examination suggests APS but clinical criterias are not met. On the other hand, with the development of basic researches, new serum antibodies have been discovered to be related to arteriovenous thrombosis and pregnancy morbidities. Those new biomarkers could help physicians enhance risk assessment and treatment decision for patients with adequate clinical manifestations for the classification criteria but negative laboratory tests, also known as seronegative APS (ANAPS). This article would spread out extra-criteria manifestations and non-criteria antiphospholipid antibodies associated with APS.

【Key words】 Antiphospholipid syndrome (APS); Extra-criteria manifestations; Non-criteria antiphospholipid antibodies; Seronegative APS (SNAPS)

· 综 述 ·

系统性红斑狼疮患者的围妊娠期管理

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【摘要】 系统性红斑狼疮 (SLE) 是一种威胁育龄期女性生殖健康的慢性、多系统的自身免疫性疾病, 其对母体、胎儿的不良影响给临床医生提出了巨大挑战。有效的孕前风险评估、合理的孕期监测及各个时期的合理用药对于 SLE 患者母、胎健康至关重要。本文讨论了 SLE 与妊娠之间的相互影响、妊娠期风险评估和病情监测, 归纳了抗风湿药物的围妊娠期使用安全性, 以便于临床上更好地指导 SLE 患者的妊娠。

【关键词】 系统性红斑狼疮 (SLE); 妊娠; 风险评估; 妊娠并发症; 药物治疗

· 综 述 ·

Management of women with systemic lupus erythematosus around the time of pregnancy Song Yufan,

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【Abstract】 Systemic lupus erythematosus (SLE) is a chronic and multi-systemic autoimmune disease, which most commonly strikes women in their childbearing age and puts forward a tremendous challenge to clinicians concerning its negative effect to mother and fetus. Effective risk evaluation, appropriate pregnancy monitoring and medical treatment are of crucial importance for the health of SLE mother and fetus. Through our review, we conclude the interaction between SLE and pregnancy, risk evaluation and disease monitoring of SLE, as well as the security of anti-rheumatic drugs around the time of pregnancy so as to clinically guide SLE women to get pregnancy successfully.

【Key words】 Systemic lupus erythematosus (SLE); Pregnancy; Risk evaluation; Pregnancy complications; Medical treatment

· 综 述 ·

子宫内膜异位症临床预测因素研究进展

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【摘要】 子宫内膜异位症 (endometriosis, EMS) 好发于育龄妇女, 常导致盆腔疼痛与不孕等。EMS 从症状出现到诊断平均需耗时 3.3~12.1 年, 可能与对疾病的本质认知不足以及缺乏敏感的血清学标志物等有关。近年来, 综合分析患者疼痛程度、不孕情况、手术史等构建的预测模型在加快 EMS 早期诊断方面起到积极推动作用。本文从早期诊断预测的角度综述了 EMS 患者的典型症状与体征、实验室检查、影像学检查及相关模型研究的最新进展, 期待通过有效的临床预测使患者得到及早诊治。

【关键词】 子宫内膜异位症 (EMS); 延迟诊断; 临床表现; 血清标志物; 预测模型

· 综 述 ·

Progress on predictive factors for the diagnosis of endometriosis *IM Min Ah, Yi Xiaofang*

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【Abstract】 Endometriosis (EMS) is a common disease affecting women of reproductive age. It may cause pelvic pain, infertility and decreased quality of life. Since it is difficult to diagnosis at early onset, the average time delayed from onset of symptoms until diagnosis of EMS is 3.3–12.1 years. The poor understanding of its pathogenetic mechanism and the scarcity of sensitive blood biomarkers are associated with this delay of diagnosis for EMS. In recent years, predictive models based on pain, infertility and operation history, etc., boost up the progress in this field. This article reviews the latest progress on the clinical manifestations of EMS, serum markers and predictive models, in order to provide some new ideas and new information to help early diagnosis of EMS.

【Key words】 Endometriosis (EMS); Delayed diagnosis; Clinical manifestation; Blood biomarker; Predictive model

· 综 述 ·

针灸在体外受精 - 胚胎移植过程中的应用研究进展

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【摘要】 现代辅助生殖技术 (assisted reproductive technology, ART) 为越来越多不孕不育夫妇解决生育问题的同时, 其高额的费用、卵巢过度刺激综合征 (ovarian hyperstimulation syndrome, OHSS) 等副作用、较低的临床妊娠率等诸多问题仍待解决。针灸作为中医学中最具代表性的治疗方式和手段, 被国内外学者关注, 并广泛应用于体外受精 - 胚胎移植 (*in vitro* fertilization-embryo transfer, IVF-ET) 治疗过程中。本文综述了 IVF-ET 联合针灸治疗改善子宫膜容受性、提高冻融胚胎移植 (frozen-thawed embryo transfer, FET) 成功率、增加妊娠机会、降低 OHSS 发生概率、可能提高活产率等方面。

【关键词】 针灸; 体外受精 - 胚胎移植 (IVF-ET); 疗效; 综述

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· 综 述 ·

Application of acupuncture and moxibustion in *in vitro* fertilization-embryo transfer Xia Qingchang,

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【Abstract】 Modern assisted reproductive technology (ART) is a problem for more and more infertile couples to solve fertility problems. There are problems still to be resolved, such as high cost, side effects such as ovarian hyperstimulation syndrome (OHSS), and low clinical pregnancy rate. As the most representative treatment and method in Chinese medicine, acupuncture has attracted the attention of scholars at home and abroad, and is widely used in the treatment of *in-vitro* fertilization-embryo transfer (IVF-ET). This article reviews that IVF-ET combined with acupuncture treatment, improves endometrial receptivity from acupuncture, improves the success rate of frozen-thawed embryo transfer (FET), increases the chance of pregnancy, and reduces occurrence rate of OHSS, possibly improves the live birth rate.

【Key words】 Acupuncture; *In vitro* fertilization-embryo transfer (IVF-ET); Curative effect; Review

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