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复旦大学附属妇产科医院

编 辑

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

总编辑

乔 杰

编辑部主任

王 健

出 版

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Editing

Editorial Board of Chinese Journal of Reproduction and Contraception
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Fax: 0086-21-64438975
Email: rande@sibpt.com
<http://zhshzybyzz.yiigle.com>

Editor-in-Chief

Qiao Jie

Managing Director

Wang Jian

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反复妊娠丢失的男性因素评估与管理中国专家共识

中国医师协会生殖医学专业委员会生殖男科学组反复妊娠丢失的男性因素评估与管理中国专家共识编写组

通信作者: 熊承良, Email: clxiong951@sina.com, 电话: +86-27-

82742288; 康跃凡, Email: fkyf@163.com, 电话: +86-591-87556044;

唐运革, Email: tyg813@126.com, 电话: +86-20-87696536

【摘要】 反复妊娠丢失 (recurrent pregnancy loss, RPL) 是一种临床常见的生育问题, 其病因较为复杂, 是一个涉及多种因素的疾病。近年来随着研究的不断深入, 越来越多的证据证明男性因素在其发生过程中同样发挥着不容忽视的作用。鉴于此, 中国医师协会生殖医学专业委员会生殖男科学组组织了生殖男科领域的专家, 从染色体异常、精液参数、精子非整倍性以及一些基因的多态性和精子的表观遗传等方面的评估和临床管理进行了深入地探讨。推荐针对 RPL 夫妇中的男性也进行染色体核型分析, 并合理选择胚胎植入前遗传学检测等; 建议进行精子 DNA 碎片率检测, 并依据病因进行适当的干预; 建议可以考虑进行精子的单倍体检测等进一步探索 RPL 中男性因素等。本共识可为从事生殖医学、男科学的专业医务人员提供建议。

【关键词】 反复妊娠丢失; 男性因素; 评估; 临床管理; 专家共识

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Chinese expert consensus on the assessment and management of male factors in recurrent pregnancy loss

Chinese Expert Consensus Compilation Group for Assessment and Management of Male Factors in Recurrent Pregnancy Loss, Reproductive Andrology Group, Reproductive Medicine Professional Committee of Chinese Medical Doctor Association

Corresponding authors: Xiong Chengliang, Email: clxiong951@sina.com, Tel: +86-27-82742288; Kang Yuefan, Email: fjkyf@163.com, Tel: +86-591-87556044; Tang Yunge, Email: tyg813@126.com, Tel: +86-20-87696536

【Abstract】 Recurrent pregnancy loss (RPL) is one of the common clinical fertility problems, which is a complex disease involving many factors with diverse causes. With the deepening of research in recent years, increasing evidence has also established that male factors also play a crucial role in RPL. Therefore, the Reproductive Andrology Group of the Professional Committee of Reproductive Medicine of the Chinese Medical Doctor Association organized experts in the field of reproductive andrology to conduct in-depth discussion on the assessment and clinical management of male factors, including chromosomal abnormalities, semen parameters, sperm aneuploidy, polymorphisms of some genes and epigenetic inheritance of sperm, etc. It is recommended to perform karyotype analysis for male of RPL couples, and to choose preimplantation genetic testing reasonably. Sperm DNA fragmentation test is recommended, and appropriate interventions based on causes are recommended. It is recommended to consider sperm haploid testing, etc. to further explore the male factor of RPL. This consensus can provide recommendations for health providers engaged in reproductive medicine and andrology.

【Key words】 Recurrent pregnancy loss; Male factors; Assessment; Clinical management; Expert consensus

Fund program: National Key Research and Development Program (2018YFC1004601); National Science and Technology Support Program (2012BAI32B03); Key Research and Development Program of Hubei Province (2022BCA042)

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睾丸显微取精术围手术期管理中国专家共识

中国医师协会生殖医学专业委员会生殖男科学组睾丸显微取精术围手术期管理中国专家共识编写组

通信作者：熊承良，Email: clxiong951@sina.com，电话：+86-27-

82742288; 康跃凡，Email: fjkylf@163.com，电话：+86-591-87556044;

洪锴，Email: kenhong99@hotmail.com，电话：+86-13501213023

【摘要】 睾丸显微取精术是非梗阻性无精子症患者获取精子的重要手术方式，已在全国多家生殖医学中心开展并取得显著的临床效果。目前，该手术围手术期管理缺乏统一的共识及标准。为提高手术的获精率，改善辅助生殖技术的临床结局，中国医师协会生殖医学专业委员会生殖男科学组成立编写专家组共同撰写本共识。本共识总结国内外临床证据，遵循循证医学原则，从术前、术中和术后管理的角度提出原则性、方向性的建议，为正在开展或准备开展睾丸显微取精术的生殖中心提供指导和帮助。

【关键词】 睾丸显微取精术； 非梗阻性无精子症； 围手术期管理； 专家共识

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Chinese expert consensus on the perioperative management of testicular microsection

Chinese Expert Consensus Compilation Group for Perioperative Management of Testicular Microsection, Reproductive Andrology Group, Reproductive Medicine Professional Committee of Chinese Medical Doctor Association

Corresponding authors: Xiong Chengliang, Email: clxiong951@sina.com, Tel: +86-27-82742288; Kang Yuefan, Email: fjkylf@163.com, Tel: +86-591-87556044; Hong Kai, Email: kenhong99@hotmail.com, Tel: +86-13501213023

【Abstract】 Microdissection testicular sperm extraction (micro-TESE) is an important surgical method to obtain sperm in non-obstructive azoospermia patients. It has been carried out in many reproductive medicine centers across the country and achieved remarkable clinical results. At present, there is a lack of unified consensus and standard for the perioperative management of this operation in the field of reproductive andrology. In order to improve the sperm retrieval rate (SRR) of surgery and the clinical outcome of assisted reproductive technology, the Reproductive Male Science Group of Reproductive Medicine Professional Committee of Chinese Medical Association was established to compile an expert group to jointly write this consensus. This consensus summarized the clinical evidence at home and abroad, followed the principles of evidence-based medicine, and put forward principled and directional suggestions from the perspective of preoperative, intraoperative and postoperative management. Providing guidance and assistance to reproductive centers that are carrying out or preparing to carry out micro-TESE.

【Key words】 Microdissection testicular sperm extraction; Non-obstructive azoospermia; Perioperative management; Expert consensus

Fund program: National Key Research and Development Program
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男性不育症的内分泌治疗中国专家 共识

中国医师协会生殖医学专业委员会生殖男科学组男性不育症的内分泌
治疗中国专家共识编写组

通信作者: 熊承良, Email: clxiong951@sina.com, 电话: +86-27-

82742288; 谷翊群, Email: yqgu90@126.com, 电话: +86-10-62148629;

康跃凡, Email: fjkylf@163.com, 电话: +86-591-87556044

【摘要】 内分泌因素是导致男性不育的重要原因之一, 而内分泌治疗是改善男性生育能力的重要手段。本共识由中国医师协会生殖医学专业委员会生殖男科学组组织专家编写, 从男性不育症的内分泌因素及分类、男性生殖内分泌的调控、常用的内分泌药物及相关制剂、常用的内分泌治疗方案以及内分泌治疗的展望等多个方面进行了深入的探讨。此外, 针对男性不育症的不同病因或不同临床表现, 本文提出了广泛认可的内分泌治疗策略。本共识的建立有助于规范男性不育症的内分泌治疗, 为从事生殖男科的专业医务人员提供专家建议。

【关键词】 不育, 男性; 内分泌因素; 内分泌治疗; 生殖男科学; 专家共识

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Chinese expert consensus on endocrine therapy of male infertility

Chinese Expert Consensus Compilation Group for Endocrine Therapy of Male Infertility, Reproductive Andrology Group, Reproductive Medicine Professional Committee of Chinese Medical Doctor Association

Corresponding authors: Xiong Chengliang, Email: clxiong951@sina.com, Tel: +86-27-82742288; Gu Yiqun, Email: yqgu90@126.com, Tel: +86-10-62148629; Kang Yuefan, Email: fjkyf@163.com, Tel: +86-591-87556044

【Abstract】 Endocrine disorder is one of the important causes of male infertility, and endocrine therapy can help improve male fertility. This consensus was prepared by experts from the Reproductive Andrology Group of the Reproductive Medicine Special Committee of the Chinese Medical Association. Here, we discussed in depth the endocrine factors and classification of male infertility. We also discussed the regulation of male reproductive endocrine, commonly used endocrine drugs and related preparations, commonly used endocrine treatment schemes and the prospect of endocrine treatment. In addition, according to the different causes or clinical features of male infertility, this paper put forward widely recognized endocrine treatment schemes. The establishment of this consensus will help regulate the endocrine treatment of male infertility and provide expert advice for medical personnel engaged in reproductive medicine or andrology.

【Key words】 Infertility, male; Endocrine factor; Endocrine therapy; Reproductive andrology; Expert consensus

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逆行射精症诊疗中国专家共识

中国医师协会生殖医学专业委员会生殖男科学组逆行射精症诊疗中国专家共识编写组

通信作者：熊承良，Email: clxiong951@sina.com，电话：+86-27-82742288；洪锴，Email: kenhong99@bjmu.edu.cn，电话：+86-10-82267521；贺小进，Email: hxj0117@126.com，电话：+86-551-62923243

【摘要】 逆行射精症是指射精时精液完全或者部分逆行进入膀胱，而导致完全无精液射出或者仅部分精液从尿道口射出的一种射精功能障碍，对于男性生育能力和性功能均会造成不利的影响。中国医师协会生殖医学专业委员会生殖男科学组组织了生殖男科领域的专家，从逆行射精症的定义、分类、病因、发病机制、诊断、鉴别诊断、治疗和助孕策略等方面进行了深入的探讨。推荐针对精液量少的男性进行射精后的尿液检查排除不完全性逆行射精症；推荐疑似逆行射精症患者进行糖尿病筛查；推荐拟交感神经药和抗胆碱能药用于逆行射精症的尝试性治疗；推荐对不同类型逆行射精症采用不同的取精方式获取精子用于人工辅助生殖技术助孕等。本共识可为从事男科学、生殖医学和辅助生殖技术的专业医务人员提供专业咨询和建议。

【关键词】 射精； 紊乱； 诊断； 治疗； 专家共识

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Chinese expert consensus on the diagnosis and treatment of retrograde ejaculation

Chinese Expert Consensus Compilation Group for Diagnosis and Treatment of Retrograde Ejaculation, Reproductive Andrology Group, Reproductive Medicine Professional Committee of Chinese Medical Doctor Association

Corresponding authors: Xiong Chengliang, Email: clxiong951@sina.com, Tel: +86-27-82742288; Hong Kai, Email: kenhong99@bjmu.edu.cn, Tel: +86-10-82267521; He Xiaojin, Email: hxj0117@126.com, Tel: +86-551-62923243

【Abstract】 Retrograde ejaculation is a kind of ejaculation dysfunction in which the semen completely or partially retrogradely enters into the bladder during ejaculation, resulting in no semen or only part of the semen being ejaculated from the external urethral orifice. Retrograde ejaculation is an important cause of male infertility and sexual dysfunction. The Reproductive Andrology Group of the Professional Committee of Reproductive Medicine of the Chinese Medical Doctor Association organized experts in the field of reproductive andrologist to conduct in-depth discussions on the definition, classification, etiology, pathogenesis, diagnosis, differential diagnosis and clinical treatment of retrograde ejaculation. Post-ejaculation urine test is recommended for men with low semen volume to identify incomplete retrograde ejaculation; diabetes screening is recommended for patients with suspected retrograde ejaculation; sympathomimetics and anticholinergics are recommended for treatment of retrograde ejaculation. It is also recommended to use different methods to retrieve sperm for assisted reproductive technology to rescue

infertility. This consensus can provide expert consultation and advice for medical professionals engaged in reproductive medicine and andrology.

【 Key words 】 Ejaculation; Disorders; Diagnosis; Treatment; Expert consensus

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·临床研究·

环孢素 A 对 IVF/ICSI 中不明原因反复种植失败患者临床疗效的回顾性分析

成伟¹ 吴亚男¹ 吴惠华¹ 邹琴燕¹ 李红¹ 朱蕊²

¹ 南京医科大学附属苏州医院 苏州市立医院生殖与遗传中心, 苏州

215002; ² 南京医科大学姑苏学院, 苏州 215004

通信作者: 朱蕊, Email: summerrui2006@aliyun.com, 电话: +86-

13382500674

【摘要】 目的 探讨环孢素 A (cyclosporine A, CsA) 对体外受精/卵胞质内单精子注射 (*in vitro* fertilization/intracytoplasmic sperm injection, IVF/ICSI) 周期不明原因反复种植失败 (unexplained repeated implantation failure, URIF) 患者再次胚胎移植临床结局的影响。方法 采用回顾性队列研究对 2016 年 4 月至 2020 年 3 月期间在南京医科大学附属苏州医院生殖与遗传中心接受胚胎移植的 IVF/ICSI 周期 URIF 患者资料进行分析, 接受 CsA 治疗 (CsA 组) 的 94 个周期, 按年龄、体质指数 (body mass index, BMI)、基础卵泡刺激素 (follicle-stimulating hormone, FSH)、移植优质胚胎数和胚胎期别配对选取未接受 CsA 的对照组 188 个周期, 比较两组患者的一般情况、移植周期特征、临床结局、产科及新生儿结局, 并对 CsA 与临床结局进行回归分析。结果 ①两组的年龄、BMI、基础 FSH、不孕年限、不

孕原因、既往失败次数、移植优质胚胎数、囊胚移植率等基线特征差异均无统计学意义（均 $P>0.05$ ），再次移植周期的胚胎数、优质胚胎数、囊胚移植率和移植日子宫内膜厚度差异均无统计学意义（均 $P>0.05$ ）。②CsA 组的胚胎种植率 [53.39%（63/118）]、临床妊娠率 [58.51%（55/94）]、活产率 [45.74%（43/94）] 明显高于对照组 [38.43%（93/242）、45.74%（86/188）、33.51%（63/188）]，差异均有统计学意义（ $P=0.007$ 、 $P=0.043$ 、 $P=0.046$ ）；CsA 组和对照组的流产率、异位妊娠率差异均无统计学意义（均 $P>0.05$ ）。③两组早产率、双胞胎率、产科并发症率、新生儿并发症率差异均无统计学意义（均 $P>0.05$ ），两组均未观察到出生缺陷。④logistic 回归分析结果显示，在纠正了年龄、BMI、基础 FSH、移植优质胚胎数和移植日子宫内膜厚度后，CsA 仍是 URIF 患者临床妊娠（校正后 $OR=1.694$ ，95% CI : 1.019~2.816， $P=0.042$ ）和活产（校正后 $OR=1.700$ ，95% CI : 1.012~2.853， $P=0.045$ ）的独立促进因素。结论 CsA 显著提高了 URIF 患者再次胚胎移植的胚胎种植率、临床妊娠率和活产率，并且不增加产科和儿科并发症的风险。CsA 可能是 URIF 患者的一种有效的治疗手段。

【关键词】 环孢素 A； 不明原因反复种植失败； 胚胎种植率； 临床妊娠率； 活产率

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A retrospective analysis of the clinical outcomes of cyclosporine A in the treatment of patients with unexplained repeated implantation failure during IVF/ICSI cycles

Cheng Wei¹, Wu Yanan¹, Wu Huihua¹, Zou Qinyan¹, Li Hong¹, Zhu Rui²

¹ Center for Human Reproduction and Genetics, the Affiliated Suzhou Hospital of Nanjing Medical University, Suzhou Municipal Hospital, Suzhou 215002, China; ² Gusu School, Nanjing Medical University, Suzhou 215004, China

Corresponding author: Zhu Rui, Email: summerrui2006@aliyun.com, Tel: +86-13382500674

【Abstract】 Objective To explore the effects of cyclosporine A (CsA) on the clinical outcomes of patients with unexplained repeated implantation failure (URIF) undergoing *in vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI) cycles. **Methods** A retrospective cohort study was conducted, and the data of URIF patients at the Center for Human Reproduction and Genetics of the Affiliated Suzhou Hospital of Nanjing Medical University from April 2016 to March 2020 was analyzed. Totally 94 cycles with CsA application were enrolled, and 188 cycles of control group were selected according to age, body mass index (BMI), basal follicle-stimulating hormone (FSH), the number of high-quality embryos transferred and embryo stage matched with CsA group. The general conditions, characteristics of previous failed transfer cycles and the *de novo* transfer cycles, clinical outcomes, obstetric and neonatal complications were compared between the two groups, and regression analysis of CsA and clinical outcomes. **Results** 1) There were no statistical differences between the two groups in baseline characteristics such as age, BMI, basal FSH, duration of infertility, indications for IVF/ICSI, number of previous failed

cycles, number of high-quality embryos and blastocyst transferred rate (all $P>0.05$). There were also no significant differences in the number of embryos transferred, the number of high-quality embryos, the rate of transferred blastocyst and the endometrial thickness on transfer day of the *de novo* transfer cycles (all $P>0.05$). 2) The embryo implantation rate, the clinical pregnancy rate and the live birth rate in CsA group [53.39% (63/118), 58.51% (55/94), 45.74% (43/94)] were distinctly higher than those of control group [38.43% (93/242), 45.74% (86/188), 33.51% (63/188)]. The differences were statistically significant ($P=0.007$, $P=0.043$, $P=0.046$). While there were no differences in miscarriage rate and ectopic pregnancy rate between the two groups (all $P>0.05$). 3) The differences of the rates of preterm birth, multiple pregnancy, obstetric and neonatal complications were all not statistically significant between the two groups (all $P>0.05$). No birth defects were observed in both groups. 4) The multivariate logistic regression analysis showed that CsA was an independent promoter of clinical pregnancy (after adjusted $OR=1.694$, 95% $CI:1.019-2.816$, $P=0.042$) and live birth (after adjusted $OR=1.700$, 95% $CI:1.012-2.853$, $P=0.045$) in URIF patients after adjusting for age, BMI, basal FSH, the number of embryos transferred and the endometrial thickness on transfer day. **Conclusion** CsA showed remarkably enhancement on embryo implantation rate, clinical pregnancy rate and live birth rate of *de novo* embryo transfer in patients with URIF, without increasing the risk of obstetric and pediatric complications. CsA application may be used as an effective treatment for URIF patients.

【Key words】 Cyclosporine A; Unexplained repeated implantation failure; Implantation rate; Clinical pregnancy rate; Live birth rate

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·临床研究·

温经汤治疗寒凝血瘀型子宫内膜异位症的临床观察: 一项随机对照研究

钟雨青¹ 曹阳¹ 庄梦斐¹ 谭丽¹ 黄圣惠¹ 杜尘¹ 周晓瑜¹ 张
婷婷¹ 孙兆贵²

¹上海中医药大学附属岳阳中西医结合医院妇科, 上海 200437; ²上海市生物医药技术研究院, 国家卫生健康委员会计划生育药具重点实验室,
上海 200032

通信作者: 张婷婷, Email: tingting185@aliyun.com, 电话: +86-21-
65161782

【摘要】 目的 探究《金匱要略》温经汤治疗寒凝血瘀型子宫内膜异位症的临床疗效。方法 采用随机对照试验, 选取 2018 年 12 月至 2021 年 1 月期间在上海中医药大学附属岳阳中西医结合医院妇科就诊的寒凝血瘀型子宫内膜异位症患者 90 例, 以随机数字表法将研究对象随机分为对照组和治疗组各 45 例。治疗组采用温经汤治疗, 对照组予以安慰剂(10%浓度温经汤)。两组均为月经第 1 天起口服, 连服 14 d 为一个疗程, 共 3 个疗程。通过主观评价两组患者治疗前后主要观察指标: 痛经症状、中医证候评分, 次要观察指标: 月经情况、简氏麦吉尔疼痛问卷(short form McGill pain questionnaire, SF-MPQ)评分。采用酶联免疫吸附测定法(enzyme-linked immunosorbent assay, ELISA)测定血清人白细胞介素-8(interleukin-8, IL-8)、肿瘤坏死因子- α (tumor necrosis factor- α , TNF- α)、前列腺素 F2 α (prostaglandin F2 α , PGF2 α)水平的变化, 判定临床疗效及中医证候疗效。结果 本研究过程中共脱落患者 7 例, 包括治疗组 1 例和对照组 6 例。最后实际观察病例数 83 例(治疗组 44 例、对照组 39 例)。临床疗效方面治疗组有效率[75.00% (33/44)]显著高于对照组[23.08% (9/39), $P<0.001$]; 中医证候疗效方面治疗组[70.45% (31/44)]显著高于对照组[20.51% (8/39), $P<0.001$]。治疗后, 治疗组月经情况[2.00 (1.00, 4.00)分]、痛经症状[7.25 (5.00, 9.88)分]、SF-MPQ[10.00 (4.50, 18.00)分]、中医证候评分[13.50 (9.25, 20.00)分]及 IL-8 水平[9.80 (5.73, 27.53) ng/L]、TNF- α 水平[5.05 (4.10, 6.20) ng/L]、PGF2 α 水平[147.16 \pm 22.24 ng/L]均较对照组显著下降[4.00 (2.00, 6.00)分, $P=0.022$; 8.00 (6.50, 12.00)分, $P=0.030$; 13.00 (4.00, 24.00)分, $P<0.001$; 17.00 (9.00, 26.00)分, $P<0.001$; 18.20 (10.00, 30.90) ng/L, $P=0.013$; 5.80 (4.50, 10.70) ng/L, $P=0.035$; (165.17 \pm 30.33) ng/L, $P=0.001$]。结论 温经汤能够改善寒凝血瘀型子宫内膜异位症患者的中医证候, 临床疗效确切, 其机理可能涉及增强机体免疫力, 缓解子宫平滑肌收缩。

【关键词】 子宫内膜异位症; 随机对照试验; 温经汤; 寒凝血瘀证

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Clinical observation on treating endometriosis with cold coagulation and blood stasis syndrome by Wenjing Decoction: a randomized controlled trial

Zhong Yuqing¹, Cao Yang¹, Zhuang Mengfei¹, Tan Li¹, Huang Shenghui¹, Du Chen¹, Zhou Xiaoyu¹, Zhang Tingting¹, Sun Zhaogui²

¹ Gynaecology Department, Yueyang Hospital of Integrative Medicine Affiliated to Shanghai University of Traditional Chinese Medicine, Shanghai 200437, China; ² NHC Key Lab of Reproduction Regulation (Shanghai Institute for Biomedical and Pharmaceutical Technologies), Shanghai 200032, China

Corresponding author: Zhang Tingting, Email: tingting185@aliyun.com, Tel: +86-21-65161782

【Abstract】 Objective To explore the clinical effects of Wenjing Decoction in treating endometriosis syndrome with cold coagulation and blood stasis. **Methods** A randomized controlled trial was performed. A total of 90 cases were collected and with distributed random number method of drugs were divided into control group and the treatment group with 45 cases each. The treatment group was given Wenjing Decoction granules, while control group was given placebo (10% Wenjing Decoction). Both groups were taken for 14 consecutive days from the first day of menstruation as a course of 1, a total of 3 courses. Before and after treatment, main observation indexes including dysmenorrhea, Traditional Chinese Medicine (TCM) syndromes and the secondary outcome including scores of menstruation, short form McGill pain questionnaire (SF-MPQ) were detected by subjective evaluation, interleukin-8 (IL-8), tumor necrosis factor- α (TNF- α), and prostaglandin F2 α (PGF2 α) level in human serum tissue were evaluated by enzyme linked immunosorbent assay and the clinical and TCM syndromes specific effects were determined. **Results** Totally 7 patients were lost, including 1 case in the treatment group and 6 cases in control group. The number of actual observation cases was 83 (44 cases in the treatment group and 39 cases in control group). The clinical effective rate in the treatment group [75.00% (33/44)] was statistically higher than that in control group [23.08% (9/39), $P < 0.001$]. As for therapeutic effect of TCM syndromes, the effective rate in the treatment group [70.45% (31/44)] was obviously higher than that in control group [20.51% (8/39), $P < 0.001$]. After treatment, compared with the results of control group, menstruation [2.00 (1.00,4.00)], dysmenorrhea [7.25 (5.00,9.88)], SF-MPQ [10.00 (4.50,18.00)], TCM syndromes [13.50 (9.25, 20.00)] and the data of IL-8 [9.80 (5.73,27.53) ng/L], TNF- α [5.05 (4.10,6.20) ng/L] and PGF2 α [(147.16 \pm 22.24) ng/L] in the treatment group were decreased obviously [4.00 (2.00,6.00), $P = 0.022$; 8.00 (6.50,12.00), $P = 0.030$; 13.00 (4.00,24.00), $P < 0.001$; 17.00 (9.00, 26.00), $P < 0.001$; 18.20 (10.00,30.90) ng/L, $P = 0.013$; 5.80 (4.50,10.70) ng/L, $P = 0.035$; (165.17 \pm 30.33) ng/L, $P = 0.001$]. **Conclusion** Wenjing Decoction can treat TCM syndromes of endometriosis patients with cold coagulation and blood stasis, and the clinical curative effect was significant. The mechanism may involve enhancing immunity and relieving uterine smooth muscle contraction.

【 Key words 】 Endometriosis; Randomized controlled trial; Wenjing Decoction; Cold coagulation and blood stasis syndrome

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·临床研究·

辅助生殖和自然受孕女性围产期心理健康的差异: 一项前瞻性队列研究

王予¹ 李骋² 刘含¹ 张晨² 陈磊¹ 黄荷凤² 李红¹ 吴琰婷²

¹上海交通大学医学院附属国际和平妇幼保健院妇科内分泌与生殖医学

科 上海市胚胎源性疾病重点实验室, 上海 200030; ² 复旦大学附属

妇产科医院妇科内分泌与生殖医学科, 上海 200011

通信作者: 吴琰婷, Email: yanting_wu@163.com, 电话: +86-

17321218018; 李红, Email: 2750074682@qq.com, 电话: +86-

18017316035

【摘要】 目的 比较辅助生殖技术(assisted reproductive technology, ART)受孕的女性和自然受孕的女性在围产期心理健康状况的差异。方法 基于一项前瞻性的中国国家出生队列建设, 将 2017 年 3 月至 2021 年 3 月期间于上海交通大学医学院附属国际和平妇幼保健院分娩的 2 693 名研究对象纳入本次分析。根据受孕方式将研究对象分为辅助生殖(ART 组, $n=733$)和自然受孕(natural conception, NC, 记为 NC 组, $n=1960$)。在妊娠早期(<14 周)、妊娠中期(22~26 周)及妊娠晚期(30~34 周), 均采用流行病学研究中心抑郁量表(Center for

Epidemiologic Studies Depression Scale, CESD)、焦虑自评量表(Self-rating Anxiety Scale, SAS)和压力知觉量表(Perceived Stress Scale, PSS)评估妊娠期心理健康状况;在产后6周,采用爱丁堡产后抑郁量表(Edinburgh Postnatal Depression Scale, EPDS)评估产后的心理健康状况。logistic回归分析孕产妇心理健康状况相关的影响因素。结果 logistic回归结果显示,与NC组的女性相比,ART组的女性在妊娠期和产后发生抑郁症状的风险均降低:妊娠早期(aOR=0.81, 95% CI: 0.66~0.99, $P=0.043$)、妊娠中期(aOR=0.73, 95% CI: 0.60~0.90, $P=0.003$)、妊娠晚期(aOR=0.82, 95% CI: 0.68~1.00, $P=0.045$)、产后6周(aOR=0.57, 95% CI: 0.43~0.75, $P<0.001$)。同时,ART组的女性在妊娠期感受到的压力明显低于NC组(妊娠早期, $P<0.001$;妊娠中期, $P<0.001$;妊娠晚期, $P=0.001$)。而两组之间的女性在妊娠期焦虑症状的差异均无统计学意义(均 $P>0.05$)。结论 与自然受孕的女性相比,ART助孕的女性在围产期发生心理健康问题的风险较低。

【关键词】 心理健康; 围产期; 生殖技术, 辅助; 自然受孕

基金项目: 国家重点研发计划(2021YFC2700701);上海市2020年度“科技创新行动计划”学术带头人(青年)(20XD1424100)

临床试验注册: 中国临床试验注册中心, ChiCTR1900027447

Comparison of perinatal psychological distress between women conceiving spontaneously and through assisted reproductive technology: a longitudinal and prospective cohort study

Wang Yu¹, Li Cheng², Liu Han¹, Zhang Chen², Chen Lei¹, Huang Hefeng², Li Hong¹, Wu Yanting²

¹ Department of Gynecological Endocrinology and Reproductive Medicine, International Peace Maternity and Child Health Hospital, Shanghai Jiao Tong University, School of Medicine; Shanghai Key Laboratory of Embryo Original Diseases, Shanghai 200030, China; ² Department of Gynecological Endocrinology and Reproductive Medicine, Obstetrics and Gynecology Hospital, Fudan University, Shanghai 200011, China

Corresponding authors: Wu Yanting, Email: yanting_wu@163.com, Tel: +86-17321218018; Li Hong, Email: 2750074682@qq.com, Tel: +86-18017316035

【Abstract】 **Objective** To compare the perinatal mental health status of women conceived through assisted reproductive technology (ART) and women conceived naturally. **Methods** In a prospective China National Birth Cohort study, 2 693 pregnant women were enrolled in the International Peace Maternity and Child Health Hospital, Shanghai Jiao Tong University, School of Medicine from March 2017 to March 2021. They were divided into ART group ($n=733$) and natural conception (NC group, $n=1\ 960$) according to the mode of conception. Mental health was assessed in the first trimester (<14 weeks), the second trimester (22–26 weeks), and the third trimester (30–34 weeks) as well as 6 weeks after delivery. Antenatally, mental health status was assessed by using the Center for Epidemiologic Studies Depression Scale (CESD), Self-rating Anxiety Scale (SAS), and Perceived Stress Scale (PSS). Postpartum depressive symptoms were assessed using the Edinburgh Postnatal Depression Scale (EPDS). Logistic regression was used to analyze maternal mental health related factors. **Results** Logistic regression results showed that

women in the ART group were less likely to experience depressive symptoms compared with those in the NC group in the first trimester (aOR=0.81, 95% CI: 0.66–0.99), the second trimester (aOR=0.73, 95% CI: 0.60–0.90), the third trimester (aOR=0.82, 95% CI: 0.68–1.00) and 6 weeks after delivery (aOR=0.57, 95% CI: 0.43–0.75). Meanwhile, women in the ART group felt significantly less stress during pregnancy than women in the NC group (the first trimester, $P<0.001$; the second trimester, $P<0.001$; the third trimester, $P=0.001$). However, the difference in women's anxiety symptoms during pregnancy was not found to be significant between the two groups (all $P>0.05$). **Conclusion** Women who conceived through ART have lower risks of perinatal mental health problems than those who conceived spontaneously.

【Key words】 Mental health; Perinatal period; Reproductive technology, assisted; Spontaneous conception

Fund program: National Key Research and Development Program of China (2021YFC2700701); Outstanding Youth Medical Talents of Shanghai Rising Stars of Medical Talent Youth Development Program (20XD1424100)

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·实验研究·

时差成像培养系统对小鼠胚胎发育潜能及组蛋白修饰影响的研究

李竞宇 李崇 黄国宁

重庆医科大学附属妇女儿童医院生殖医学中心 人类胚胎工程重庆市

重点实验室, 重庆 400013

通信作者: 黄国宁, Email: gnhuang217@sina.com, 电话: +86-23-

63839850

【摘要】 目的 评估时差成像培养系统 (time-lapse imaging, TLI) 对小鼠胚胎发育潜能及组蛋白表观修饰的影响。方法 选择 SPF 级雌性 ICR 小鼠, 促排卵后取成熟 M_{II} 卵子进行体外受精 (*in vitro* fertilization, IVF), 获取成功受精的合子, 分别在 TLI 和常规培养体系 (standard incubators, SI) 中进行体外培养, 记录两组胚胎的 2-细胞率、4-细胞率、8-细胞率、桑葚胚率、囊胚率和孵出率。通过

Hoechst、OCT4 及 CDX2 抗体进行免疫荧光染色，分别统计囊胚细胞总数、内细胞团数和滋养外胚层细胞数。两组囊胚移植入第 2.5 天代孕母鼠子宫，统计植入率及活胎率。通过对组蛋白 H3 第 4 位赖氨酸三甲基化（H3K4me3）、组蛋白 H3 第 9 位赖氨酸二甲基化（H3K9me2）和组蛋白 H3 第 9 位赖氨酸乙酰化（H3K9ac）的免疫荧光染色，评估两组胚胎组蛋白表观修饰情况。结果 TLI 组和 SI 组的早期胚胎发育情况、内细胞团和滋养外胚层细胞数、植入率和活胎率比较差异均无统计学意义（均 $P>0.05$ ）。两组囊胚的组蛋白 H3K4me3、H3K9me2 和 H3K9ac 的表达水平差异均无统计学意义（均 $P>0.05$ ）。结论 利用 TLI 体外培养不会影响胚胎的发育潜能以及组蛋白修饰。

【关键词】 胚胎发育； 时差成像培养系统； 植入率； 活胎率； 组蛋白修饰

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Effect of time-lapse culture on the development and histone modification of mouse embryo

Li Jingyu, Li Chong, Huang Guoning

Center for Reproductive Medicine, Women and Children's Hospital of Chongqing Medical University; Chongqing Key Laboratory of Human Embryo Engineering, Chongqing 400013, China

Corresponding author: Huang Guoning, Email: gnhuang217@sina.com, Tel: +86-23-63839850

【Abstract】 **Objective** To evaluate the effect of time-lapse imaging (TLI) culturing on the potential of mouse embryonic development and histone modification. **Methods** The matured M_{II} oocytes were obtained after superovulation, using SPF female ICR mice. The successfully fertilized zygotes through *in vitro* fertilization (IVF) were assigned to culture either in TLI or standard incubator (SI). Immunofluorescent (IF) was performed to count the number of total cells, inner cell mass (ICM) and trophoblast cells (TE) in blastocysts, using the Hoechst, the antibody of OCT4 and CDX2, respectively. The rates of 2-cell, 4-cell, 8-cell, morula, blastocyst and blastocyst hatching were recorded. The blastocysts of the two groups were transferred into uteruses of day 2.5 pseudo pregnant mice, and the implantation rate and the live fetal rate were calculated. In addition, the levels of H3K4me3, H3K9me2, and H3K9ac were compared in blastocyst between the two groups using IF. **Results** No significant differences were found in the embryonic development, the cell number of ICM and TE, the implantation rate and the live fetal rate between TLI and SI groups (all $P>0.05$). Furthermore, there were no significant differences in the level of histone modification, including H3K4me3, H3K9me2, and H3K9ac (all $P>0.05$). **Conclusion** TLI culture does not have a significant adverse impact on the embryonic development and histone modification.

【Key words】 Embryonic development; Time-lapse imaging system; Implantation; Live fetal rate; Histone modification

Fund program: Chongqing Science and Health Joint Project (2021MSXM072)

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·现场调查·

多囊卵巢综合征不孕患者备孕期间生活方式管理方案的构建

卢山¹ 孙小玲² 王静³ 张宁⁴ 孟芳芳⁵ 刘才琪⁶ 张成果⁶

¹南京中医药大学中西医结合鼓楼临床医学院, 南京 210008; ²南京大学医学院附属鼓楼医院江北门诊, 南京 210008; ³南京大学医学院附属鼓楼医院健康管理中心, 南京 210008; ⁴江苏大学医学院护理系, 镇江 212000; ⁵南京大学医学院护理系, 南京 210093; ⁶南京中医药大学护理学院, 南京 210046

通信作者：孙小玲, Email: sunxiaoling@nju.edu.cn, 电话: +86-13951719180

【摘要】 目的 构建多囊卵巢综合征 (polycystic ovary syndrome, PCOS) 不孕患者备孕期间的生活方式管理方案, 为临床实践提供参考。方法 在团队前期证据总结的基础上, 参考备孕妇女膳食指南, 初步拟定方案初稿, 并通过 2 轮德尔菲专家函询确定生活方式管理方案。结果 2 轮专家函询问卷的有效回收率为 100%, 专家权威系数分别是 0.88、0.90, 肯德尔协调系数分别是 0.18、0.22, 显著性检验 $P < 0.001$ 。最终形成包含 8 个一级条目、25 个二级条目和 81 个三级条目的生活方式管理方案。结论 基于循证和专家函询构建的 PCOS 不孕患者备孕期间的生活方式管理方案具有较强的科学性和实用性, 可为临床实践提供客观具体的实施策略。

【关键词】 多囊卵巢综合征; 孕前保健; 生活方式; 循证医学; 德尔菲技术

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Construction of lifestyle management scheme for infertile patients with polycystic ovary syndrome during pregnancy preparation

Lu Shan¹, Sun Xiaoling², Wang Jing³, Zhang Ning⁴, Meng Fangfang⁵, Liu Caiqi⁶, Zhang Chengguo⁶

¹ Nanjing Drum Tower Hospital Clinical College of Traditional Chinese and Western Medicine, Nanjing University of Chinese Medicine, Nanjing 210008, China; ² Outpatient Department, Jiangbei District, Nanjing Drum Tower Hospital, the Affiliated Hospital of Nanjing University Medical School, Nanjing 210008, China; ³ Health Management Center, Nanjing Drum Tower Hospital, the Affiliated Hospital of Nanjing University Medical School, Nanjing 210008, China; ⁴ Department of Nursing, School of Medicine, Jiangsu University, Zhenjiang 212000, China; ⁵ Department of Nursing, School of Medicine, Nanjing University, Nanjing 210093, China; ⁶ College of Nursing, Nanjing University of Chinese Medicine, Nanjing 210046, China

Corresponding author: Sun Xiaoling, Email: sunxiaoling@nju.edu.cn, Tel: +86-13951719180

【Abstract】 Objective To construct a lifestyle management scheme for infertile patients with polycystic ovary syndrome (PCOS) during pregnancy preparation, so as to provide reference for clinical practice. **Methods** Based on the summary of evidence in the early stage of the team, the first draft of the scheme was preliminarily drawn up with reference to the dietary guidelines for pregnant women. Finally, the lifestyle management scheme was determined through two rounds of Delphi expert correspondence. **Results** The effective recovery rate of the two rounds of expert correspondence questionnaire was 100%, the expert authority coefficients were 0.88 and 0.90, respectively, and the Kendall coordination coefficients were 0.18 and 0.22, respectively. The significance test was $P < 0.001$. Finally, a lifestyle management scheme including 8 first level items, 25 second level items and 81 third level items was formed. **Conclusion** The lifestyle management scheme of PCOS infertile patients during pregnancy preparation based on evidence-based and expert correspondence is scientific and practical, which can provide objective and specific implementation strategies for clinical practice.

【Key words】 Polycystic ovary syndrome; Preconception care; Life style; Evidence-based medicine; Delphi technique

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·个案报道·

取卵术后脑水肿 1 例报道与文献回顾

范丽娟¹ 蒋亦林² 文雯¹ 狄政莉³ 孙泓泓⁴ 段海霞⁵ 陈琰睿⁶

梁思瑞⁷ 周寒鹰¹

¹西北妇女儿童医院生殖中心, 西安 710000; ²北京大学人民医院神经外科, 北京 100044; ³西安市中心医院神经内科, 西安 710000; ⁴西安交通大学第二附属医院医学影像科, 西安 710000; ⁵西北妇女儿童医院生殖妇科, 西安 710000; ⁶西安医学院研究生院妇产科学系, 西安 710021; ⁷西安医学院临床医学院临床医学系, 西安 710021

通信作者: 周寒鹰, Email: Zhouhy718@126.com, 电话: +86-15398093292

【摘要】 目的 探讨控制性超促排卵(controlled ovarian hyperstimulation, COH)和经阴道超声引导下卵巢穿刺取卵术后脑水肿发生机制和治疗方法。方法 回顾分析 1 例 COH 和取卵术后脑水肿诊疗经过并进行文献复习。结果 患者采用卵泡期长效方案促排卵后获卵 30 枚, 因卵巢过度刺激综合征(ovarian hyperstimulation syndrome, OHSS)予羟乙基淀粉 500 mL 扩容。取卵术后 8 h 突发烦躁、意识模糊、呕吐, 血生化指标检查示低钠血症, 经阴道彩色超声检查示双侧卵巢增大, 内见多个囊肿; 头颅 CT 示脑水肿。高渗盐和甘露醇治疗 12 h 后患者生命体征平稳、症状缓解。取卵术后第 5 天因腹腔积液行超声引导下穿刺放腹水。取卵术后第 7 天因血浆 D-二聚体升高予低分子肝素抗凝、预防血栓。2 周后患者痊愈出院。结论 COH 和取卵术后脑水肿发生率低, 但其症状重且可能危及生命。低钠血症可能是此患者脑水肿的主要原因。

【关键词】 卵巢过度刺激综合征; 低钠血症; 脑水肿; 控制性超促排卵; 取卵术

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Brain edema after oocyte retrieval: a case report and literature review

Fan Lijuan¹, Jiang Yilin², Wen Wen¹, Di Zhengli³, Sun Honghong⁴, Duan Haixia⁵, Chen Yanrui⁶, Liang Sirui⁷, Zhou Hanying¹

¹Reproductive Medical Center, Northwest Women's & Children's Hospital, Xi'an 710000, China; ²Department of Neurosurgery, People's Hospital of Peking University, Beijing 100044, China; ³Department of Neurology, Xi'an Central Hospital, Xi'an 710000, China;

⁴ Department of Imaging, the Second Affiliated Hospital of Xi'an Jiaotong University, Xi'an 710000, China; ⁵ Department of Reproductive Gynecology, Northwest Women's & Children's Hospital, Xi'an 710000, China; ⁶ Department of Obstetrics and Gynecology, Graduate School, Xi'an Medical College, Xi'an 710021, China; ⁷ Department of Clinical Medicine, School of Clinical Medicine, Xi'an Medical College, Xi'an 710021, China
Corresponding author: Zhou Hanying, Email: Zhouhy718@126.com, Tel: +86-15398093292

【Abstract】 Objective To investigate the mechanism, treatment and prevention of brain edema after controlled ovarian hyperstimulation (COH) and transvaginal ovarian puncture and oocyte retrieval. **Methods** A retrospective clinical study and literature review were performed to analyze one patient who was diagnosed as having brain edema after COH and transvaginal ovarian puncture and oocyte retrieval. **Results** After long acting gonadotropin-releasing hormone analogue (GnRH-a) COH protocol, 30 oocytes were obtained. Hydroxyethyl starch 500 mL was given to treat ovarian hyperstimulation syndrome (OHSS) after oocyte retrieval. The patient had sudden irritability, blurred consciousness and vomiting at the 8th hour after oocyte retrieval. The examinations showed hyponatremia and brain edema. The patient relived after mannitol and hypertonic saline treatment. On the 5th day after oocyte retrieval, the patient performed paracentesis guided by ultrasound due to seroperitoneum. Low molecular weight heparin was applied to prevent thrombosis after the flare up of serum D-Dimer on the 7th day. The patient recovered and discharged after 2 weeks. **Conclusion** The incidence of brain edema after COH and transvaginal ovarian puncture and oocyte retrieval was very low. However, the symptoms may be severe and may be life-threatening.

【Key words】 Ovarian hyperstimulation syndrome; Hyponatremia; Brain edema; Controlled ovarian hyperstimulation; Oocyte retrieval

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·个案报道·

RAG1 基因新发现变异位点的结构分析及致病性预测

刘永祥¹ 段雨薇² 翁治委¹ 张淑婷¹ 李学荣¹ 彭新良¹ 周瑞鸿

³ 周少虎¹

¹广州中医药大学第一附属医院生殖医学科, 广州 510405; ²中山大学

附属第一医院生殖医学中心, 广州 510080; ³广州医药研究总院有限公

司, 广州 510220

通信作者: 周少虎, Email: zhoushaohu@vip.163.com, 电话: +86-

13802757908

【摘要】 目的 探索胚胎植入前单基因遗传学检测 (preimplantation genetic testing for monogenic, PGT-M) 周期前与重症联合免疫缺陷 (severe combined immunodeficiency, SCID) 相关的重组激活基因 1 (recombination activating gene 1, RAG1) 基因结构和功能, 并对其新发现变异位点进行致病性预测。方法 针对 2016 年 8 月于中山大学附属第一医院生殖医学中心就诊的先证者的外显子报告及其父母外周血染色体核型及 Sanger 测序数据, 利用 PROVEAN、PolyPhen-2 和 Mutation Taster 致病性预测软件对 RAG1 基因变异位点的基因结构、蛋白保守结构域进行分析, 并对突变与野生型 RAG1 蛋白的结构进行三维结构重建, 实现致病性的预测。结果 双方均为 RAG1 基因突变携带者, 突变位点位于 11 号染色体上, 女方为 c.946T>G (p.C316G) 杂合错义突变, 男方为 c.1194_1196del (p.L399del) 杂合整码突变。两个突变位点对应的氨基酸在人、黑猩猩、猪、牛、大鼠、小鼠 6 个物种中高度保守。二级三级结构重建显示, c.946T>G (p.C316G) 突变导致对应的 RING 型锌指结构丧失结合锌离子的能力, c.1194_1196del (p.L399del) 突变引起的第 399 位亮氨酸缺失导致氢键减少 1 条。结论 推测 RAG1 两个新发现变异位点为可致病性突变, 扩大了 RAG1 基因的突变谱, 具有重要的研究价值。

【关键词】 重组激活基因 1; 新发变异位点; 生物信息学; 致病性预测

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Structural analysis and pathogenicity prediction of novel discovered mutation sites of human RAG1 gene

Liu Yongxiang¹, Duan Yuwei², Weng Zhiwei¹, Zhang Shuting¹, Li Xuerong¹, Peng Xinliang¹, Zhou Ruihong³, Zhou Shaohu¹

¹ Department of Reproductive Medicine, the First Affiliated Hospital of Guangzhou University of Chinese Medicine, Guangzhou 510405, China; ² Reproductive Medicine Center, the First Affiliated Hospital of Sun Yat-sen University, Guangzhou 510080, China; ³ Guangzhou General Pharmaceutical Research Institute Company Limited, Guangzhou 510220, China

Corresponding author: Zhou Shaohu, Email: zhoushaohu@vip.163.com, Tel: +86-13802757908

【 Abstract 】 Objective To explore the structure and function of recombination activating gene 1 (RAG1) related to severe combined immunodeficiency (SCID) before entering the preimplantation genetic testing for monogenic (PGT-M) cycle, and to predict the pathogenicity of its novel mutation sites. **Methods** According to the whole exome sequencing reports of the probands in the Department of Reproductive Medicine, the First Affiliated Hospital of Sun Yat-sen University on August 2016, the chromosome karyotypes and Sanger sequencing of their parents from their peripheral blood, the structures and protein conserved domains of the novel mutation sites of RAG1 gene were analyzed by PROVEAN, PolyPhen-2 and Mutation Taster software, and the secondary and tertiary structures of the mutant and wild type RAG1 protein were reconstructed in three-dimensional structure to predict its pathogenicity. **Results** The couple were carriers of RAG1 gene mutation, which were located on chromosome 11. The female was heterozygous missense mutation of c.946T>G (p.C316G) and the male was heterozygous integer mutation of c.1194_1196del (p.L399del). The amino acid of the RAG1 mutations mentioned above were highly conserved among human, chimpanzee, pig, cattle, rats and mice. The secondary and tertiary structure reconstruction showed that the RING-type zinc finger structure lost the ability to bind zinc ions due to c.946T>G mutation, and the deletion of leucine at position 399 caused by c.1194_1196del mutation reduced one hydrogen bond. **Conclusion** It is speculated that the two novel mutation sites of RAG1 are pathogenic mutations, which expand the mutation spectrum of RAG1 gene and have important research value.

【 Key words 】 Genes, RAG1; Novel discovered mutation sites; Bioinformatics; Pathogenicity prediction

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·病案报道·

恶性肿瘤患者生育力保存的全流程管理

田培玲 窦姗姗 管一春 李嘉恒

郑州大学第三附属医院生殖中心, 郑州 450000

通信作者：窦姗姗，Email: doushanshan1992@126.com，电话：+86-15038162208

【摘要】 目的 总结恶性肿瘤患者生育力保存全流程管理经验。方法 回顾性分析 2019 年 12 月至 2022 年 9 月期间于郑州大学第三附属医院生殖中心行生育力保存的 24 例患者的临床资料及全流程管理。生育力保存患者管理要点包括初诊决策支持、就诊专人接待、保护隐私，检查全程陪同，促排卵阶段人性化管理，预防感染，心理评估及疏导，提供专业的健康教育等。结果 经过全流程精心治疗和护理，24 例患者均顺利完成生育力保存，且均未发生感染、取卵后出血等并发症。结论 为生育力保存患者进行护理时，应该综合考虑患者的身体、心理情况，为其提供更有针对性的护理服务，以满足患者的需求，达到最佳的临床效果。

【关键词】 生育力保存； 全流程管理； 护理

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Whole-process management of fertility preservation in the patients with malignant tumor

Tian Peiling, Dou Shanshan, Guan Yichun, Li Jiaheng

Reproductive Center, the Third Affiliated Hospital of Zhengzhou University, Zhengzhou 450000, China

Corresponding author: Dou Shanshan, Email: doushanshan1992@126.com, Tel: +86-15038162208

【Abstract】 Objective To summarize the experience of the whole process management of fertility preservation in patients with malignant tumor. **Methods** The clinical data and the whole-process management of 24 fertility preservation procedures in the Reproductive Center of the Third Affiliated Hospital of Zhengzhou University from December 2019 to September 2022 were retrospectively analyzed. The key points of fertility preservation patient management included decision support for initial diagnosis, specially-assigned reception, privacy protection, whole-process inspection escort, humanized management at the stage of drainage promotion, infection prevention, psychological assessment and counseling, and professional health education. **Results** After the whole process of careful treatment and nursing, all the 24 patients successfully completed fertility preservation, and no complications such as infection, bleeding after egg extraction occurred. **Conclusion** When caring for patients with fertility preservation, the physical and psychological conditions of patients should be considered comprehensively, so as to provide more targeted nursing services to meet the needs of patients and achieve the best clinical results.

【Key words】 Fertility preservation; Whole-process management; Nursing

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·综述·

双胎消失存活子代预后研究进展

李佳蓉¹ 李晶宇¹ 崔琳琳²

¹ 生殖内分泌教育部重点实验室(山东大学) 山东省生殖医学重点实验室 山东省生殖健康临床医学研究中心 国家辅助生殖与优生工程技术研究中心, 济南 250012; ² 山东大学生殖医学研究中心(山东大学第二医院), 济南 250012

通信作者: 崔琳琳, Email: fdclear3@126.com, 电话: +86-531-85651598

【摘要】 双胎消失综合征是指妊娠过程中胎儿自发性减少, 既往研究显示其在辅助生殖技术中发生率为 5%~30%。目前双胎消失现象对于孕产结局的影响还没有明确的定论。根据健康与疾病的发展起源(Developmental Origin of Health and Disease, DOHaD)理论, 生命早期暴露对成年期健康结局有深远影响。本文对既往关于双胎消失对存活子代相关研究进展进行了系统性综述, 对其健康转归和潜在机制进行了探讨, 以为辅助生殖技术相关临床策略和双胎消失暴露人群的远期健康监测提供指导性建议。

【关键词】 生殖技术, 辅助; 双胎消失综合征; 孕产结局; 新生儿结局

Research progress on prognosis of vanishing twins with assisted reproductive technology

Li Jiarong¹, Li Jingyu¹, Cui Linlin²

¹ Key Laboratory of Reproductive Endocrinology of Ministry of Education (Shandong University); Shandong Key Laboratory of Reproductive Medicine; Shandong Provincial Clinical Research Center for Reproductive Health; National Research Center for Assisted Reproductive Technology and Reproductive Genetics, Jinan 250012, China; ² Center for Reproductive Medicine of Shandong University (the Second Hospital of Shandong University), Jinan 250012, China

Corresponding author: Cui Linlin, Email: fdclear3@126.com, Tel: +86-531-85651598

【Abstract】 Vanishing twin syndrome (VTS), defined as the spontaneous reduction of a twin fetus, was estimated to occur in 5%–30% *in vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI) pregnancies. Previous studies focused on the poor perinatal outcomes of infants with vanishing co-twin, but the results were inconsistent. According to the theory of Developmental Origin of Health and Diseases (DOHaD), the environment during fetal life influences the predisposition to disease and the risk of morbidity in adulthood. This review will focus on the short- and long-term consequences for the surviving fetus and the potential mechanism of vanishing twins in IVF/ICSI pregnancies, in order to provide guiding suggestions for clinical strategies related to assisted reproductive technology and long-term health monitoring of patients diagnosed with vanishing twin syndrome.

【Key words】 Reproductive technology, assisted; Vanishing twin syndrome; Pregnancy outcome; Neonatal outcome

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·综述·

早期子宫内膜癌及子宫内膜非典型增生保守治疗后接受辅助生殖技术助孕现状及研究进展

郭亚兴 李红真 乔杰

北京大学第三医院妇产科生殖医学中心 国家妇产疾病临床医学研究中心（北京大学第三医院） 辅助生殖教育部重点实验室（北京大学）

北京市生殖内分泌与辅助生殖技术重点实验室，北京 100191

通信作者：乔杰，Email: jie.qiao@263.net，电话：+86-10-82266886

【摘要】 近年来，子宫内膜癌（endometrial carcinoma, EC）及子宫内膜非典型增生（atypical endometrial hyperplasia, AEH）的发病率较前升高，且患者呈现出年轻化趋势。对于尚未生育的年轻患者来讲，保守治疗后接受辅助生殖技术（assisted reproductive technology, ART）治疗，可以帮助她们尽快实现生育愿望。目前对于 EC 及 AEH 保守治疗后进行辅助生殖的研究逐年增多，但多为小样本研究。本文对现有研究进行综述，进而阐释 EC 及 AEH 保守治疗后进行 ART 助孕的有效性、安全性以及影响因素。

【关键词】 生殖技术，辅助； 子宫内膜癌； 子宫内膜非典型增生； 保留生育功能

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Current research of assisted reproductive technology for women with early endometrial carcinoma and atypical endometrial hyperplasia after conservative treatment

Guo Yaxing, Li Hongzhen, Qiao Jie

Center for Reproductive Medicine, Department of Obstetrics and Gynecology, Peking University Third Hospital; National Clinical Research Center for Obstetrics and Gynecology (Peking University Third Hospital); Key Laboratory of Assisted Reproduction (Peking University); Ministry of Education/Beijing Key Laboratory of Reproductive Endocrinology and Assisted Reproductive Technology, Beijing 100191, China

Corresponding author: Qiao Jie, Email: jie.qiao@263.net, Tel: +86-10-82266886

【Abstract】 In recent years, the incidence of endometrial carcinoma (EC) and atypical endometrial hyperplasia (AEH) has increased than before and showed a tendency to be younger. Meanwhile, young women diagnosed with EC or AEH have strong desires to preserve their fertilities, so that they may choose the conservative treatment. After achieving complete remission, many of them are recommended to undergo assisted reproductive technology (ART) treatment to conceive. At present, the research on ART after conservative treatment of EC and AEH is increasing year by year, but most of them are small sample studies. This article reviewed existing studies to explain the effectiveness, safety and influencing factors of ART after conservative treatment of EC and AEH.

【Key words】 Reproductive technology, assisted; Endometrial carcinoma; Atypical endometrial hyperplasia; Fertility-sparing treatment

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·综述·

小檗碱在多囊卵巢综合征治疗中的研究进展

瞿睿 王璟萱 李赛姣

武汉大学人民医院生殖医学中心 湖北省辅助生育与胚胎发育医学临床研究中心, 武汉 430060

通信作者: 李赛姣, Email: alva_w hu@hotmail.com, 电话: +86-27-88041911*82263

【摘要】 多囊卵巢综合征 (polycystic ovary syndrome, PCOS) 是育龄妇女最常见的生殖和内分泌疾病之一, 其发病机制不清, 目前尚无根治方法。PCOS 临床表现为胰岛素抵抗、高胰岛素血症、肥胖、高雄激素血症、心血管风险增加等。小檗碱是一种提取于黄连的生物碱, 具有抗炎、抗菌、降血脂、治疗胰岛素抵抗等多重功效。近年研究表明, 小檗碱在 PCOS 中调节激素水平、改善慢性炎症、胰岛素抵抗、排卵障碍和子宫内膜病变等方面的作用, 展现出较大的临床运用前景, 本文对小檗碱在 PCOS 治疗中的相关研究进展进行综述。

【关键词】 多囊卵巢综合征; 小檗碱; 胰岛素抵抗; 雄激素; 慢性炎症

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Research progress of berberine in the treatment of polycystic ovary syndrome

Qu Rui, Wang Jingxuan, Li Saijiao

Reproductive Medical Center, Renmin Hospital of Wuhan University; Hubei Clinical Research Center for Assisted Fertility and Embryo Development, Wuhan 430060, China

*Corresponding author: Li Saijiao, Email: alva_w hu@hotmail.com, Tel: +86-27-88041911*82263*

【Abstract】 Polycystic ovary syndrome (PCOS) is one of the most common reproductive and endocrine diseases in women of childbearing age. The pathogenesis of PCOS is unclear and there is no radical cure at present. Its clinical manifestations include insulin resistance (IR), hyperinsulinemia, obesity, hyperandrogenemia (HA), increased cardiovascular risk, etc. Berberine (BBR) is an alkaloid extracted from coptis, with anti-inflammatory, antibacterial, decreasing blood lipids, treatment of IR and other multiple effects. In recent years, amounts of medical literatures have reported the therapeutic effects of BBR in PCOS, including improving hormone levels, chronic inflammation, IR, ovulation dysfunction and endometrial lesions, which shows a great prospect of clinical application. In this paper, we reviewed the research progress of BBR in the treatment of PCOS.

【Key words】 Polycystic ovary syndrome; Berberine; Insulin resistance; Androgen; Chronic inflammation

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·综述·

干细胞治疗女性不孕相关疾病的研究进展

刘琳¹ 任甜甜² 刘学润² 高文欣² 曹颖² 马晓玲¹

¹ 兰州大学第一医院生殖医学专科医院 甘肃省生殖医学与胚胎重点实

验室, 兰州 730000; ² 兰州大学第一临床医学院, 兰州 730000

通信作者: 马晓玲, Email: maxl2005@163.com, 电话: +86-931-8357358

【摘要】 不孕症严重威胁育龄期妇女身心健康。随着现代医学的发展, 干细胞受到广泛关注并且逐渐被应用于医学研究中。干细胞治疗作为生殖医学领域一个新兴研究热点, 在不孕症疾病中展现出良好的治疗效果。本文对干细胞治疗在不孕症疾病方面的研究进展作一综述, 旨在为临床治疗提供新的思路。

【关键词】 间充质干细胞; 不育, 女性; 干细胞治疗

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Research progress of stem cells in the treatment of female infertility related diseases

Liu Lin¹, Ren Tiantian², Liu Xuerun², Gao Wenxin², Cao Ying², Ma Xiaoling¹

¹The Reproductive Medicine Special Hospital of the 1st hospital of Lanzhou University; Key Laboratory for Reproductive Medicine and Embryo of Gansu province, Lanzhou 730000, China; ²The First Clinical Medical College of Lanzhou University, Lanzhou 730000, China

Corresponding author: Ma Xiaoling, Email: maxl2005@163.com, Tel: +86-931-8357358

【Abstract】 Infertility has become a serious threat to the physical and mental health of women of childbearing age. With the development of modern medicine, stem cell has been widely concerned and gradually applied in medical research. As an emerging research focus in the field of reproductive medicine, stem cell therapy has shown good therapeutic effects in the treatment of infertility. This article

reviewed the research progress of stem cell therapy in infertility diseases, aiming to provide new ideas for clinical treatment.

【Key words】 Mesenchymal stem cell; Infertility, female; Stem cell therapy

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