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CONTENTS IN BRIEF

·述 评·

高龄男性生育研究的机遇与挑战

朱伟杰

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【摘要】 男性年龄增高,精子受精潜力下降和精子基因组正常性改变的风险升高,导致高龄男性生育力与生殖安全性降低。但男性生育力衰减是一个缓慢的生理过程,而且存在着很大的个体差异。现阶段我国高龄男性生育人群具有与以往时期及国外人群不同的特点。围绕男性增龄的生殖功能变化、遗传风险及其相关机制做深入研究,有助于增进对高龄男性生育的认识,更有利于优生、保障生殖健康和生殖安全。

【关键词】生育力; 高龄男性; 人类精子; 生殖安全性

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•述 评•

Opportunities and challenges on fertility for aging men

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[Abstract] Aging men may be associated with the low sperm fertilizing potential and an increased risk of paternal genome integrity, which cause impaired male fertility and may contribute to adverse reproductive outcomes. However, the decline of male fertility related to age is a very slow physiological process, and exists great individual difference. Aging men in China at the present period have unique features, which are different from the aging males lived in previous periods or foreign countries. Further investigations should be focused on changes of reproductive function and genetic risk associated with advanced paternal age and their molecular mechanisms, which would increase knowledge on male fertility for aging men and benefit to reproductive health and safety.

[Key words] Fertility; Aging man; Human sperm; Reproductive safety

Fund program: Natural Science Foundation of Guangdong Province, China (010399)

高育龄女性行胚胎植入前遗传学筛查的 妊娠结局分析

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刘培昊和李鸿昌对本文有同等贡献

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【摘要】目的 研究胚胎植入前非整倍性遗传学检测 (preimplantation genetic testing for aneuploidies,PGT-A) 对高育龄女性妊娠结局的影响。方法 选取 2015 年 1 月—2017 年 5 月期间于山东大学附属生殖医院进行第 1 周期 PGT-A 助孕的 \geq 38 岁的女性 98 例 (PGT 组),另分别选取同时间段进行体外受精 (in vitro fertilization,IVF) 及卵胞质内单精子注射 (intracytoplasmic sperm injection,ICSI) 助孕的患者作为对照组,与 PGT 组进行 1 : 2 匹配,分别比较 PGT 组与 IVF 组、ICSI 组的妊娠结局。同时观察拟行PGT-A 助孕,但因胚胎培养第 3 日 (D3) 优质胚胎数目不足取消 PGT-A 并行新鲜胚胎移植患者的妊娠结局。结果 PGT 组与对照组相比,移植周期活产率显著升高 [PGT 组 (48.44%) 比 IVF 组 (24.00%),P<0.001;PGT 组 比 ICSI 组 (27.62%),P=0.002],妊娠丢失率显著下降 [PGT 组 (22.50%) 比 IVF 组 (46.07%),P=0.011;PGT 组比 ICSI 组 (45.05%),P=0.014],但 PGT 组 98 例中,有 34 例患者因检测后无可移植胚胎放弃移植。PGT 组与对照组间患者活产率、临床妊娠率差异均无统计学意义 (P>0.05)。高育龄女性取消 PGT-A 检测、行 D3 新鲜胚胎移植后,活产率仅为 7.14%。结论 高育龄女性进行 PGT-A 助孕可显著提高活产率、降低妊娠丢失风险、增加移植效率,但周期取消率增高。另外,优质胚胎数少的高龄女性,是否取消 PGT-A 检测、行 D3 新鲜胚胎移植应权衡利弊、慎重考虑。

【关键词】 妊娠结局; 高育龄; 胚胎植入前遗传学检测; 活产率; 妊娠丢失率

Pregnancy outcome analysis of preimplantation genetic testing for women of advanced maternal age

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[Abstract] Objective To investigate whether preimplatation genetic testing for aneuploidies (PGT-A) can benefit pregnancy outcomes in women of advanced maternal age (AMA). Methods received PGT-A between January 2015 and May 2017 in Reproductive Medicine Center Shandong University were enrolled, named PGT group. Patients who underwent in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI) were matched as control group. The pregnancy outcomes were compared between PGT and IVF groups as well as between PGT and ICSI groups, respectively. We also analyzed the pregnancy outcomes of AMA women who prepared for a PGT-A cycle but changed to fresh embryo transfer because of less than 3 good-quality embryos on day 3 (D3). Results The live birth rate (LBR) per transfer was significantly higher in PGT group (48.44%) compared with IVF (24.00%, P<0.001) and ICSI group (27.62%, P=0.002). The pregnancy loss rate was significantly lower in PGT group (22.50%) compared with IVF (46.07%, P=0.011) and ICSI group (45.05%, P=0.014). But 34 of 98 transfer cycles were cancelled in PGT group as there were no normal embryos. The LBR per patient and the pregnancy rate showed no significant differences (P>0.05) between PGT group and control group. The LBR was only 7.14% in AMA women who underwent fresh embryo transfer cancelling PGT-A. For women of high reproductive age, PGT-A can significantly improve the LBR, reduce the risk of pregnancy loss and increase the efficiency of transplantation, but it will increase the cycle cancellation rate. Careful consideration is advised when an AMA woman is deciding whether to cancel PGT-A and receive fresh embryo transfer with limited number of D3 good-quality embryos.

[Key words] Pregnancy outcome; Advanced maternal age; Preimplatation genetic screening; Live birth rate; Pregnancy loss rate

高龄与非高龄患者胚胎移植术后自然流产 胚胎染色体核型异常多因素回归分析

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【摘要】目的 分析不同年龄段患者行辅助生殖技术 (assisted reproductive technology, ART) 助孕后自然 流产胚胎染色体核型异常的发生率及其相关危险因素。方法 回顾性队列分析 2016年1月—2018年6月期 间于中山大学附属第六医院生殖中心行体外受精/卵母细胞质内单精子注射-胚胎移植(in vitro fertilization/ intracytoplasmic sperm injection-embryo transfer, IVF/ICSI-ET) 后自然流产并行绒毛染色体核型检测的患 者资料。基于患者年龄,分成高龄组(≥35岁)和年轻组(<35岁),分别分析染色体核型异常胚胎在 ART 术后自然流产胚胎中所占比例。根据染色体核型检测结果,分为染色体核型异常组和正常组,进行 单因素分析及二变量逻辑回归分析,探索胚胎染色体核型异常发生的高危因素。结果 共纳入 506 例年轻 患者及 371 例高龄患者,胚胎染色体核型异常率分别为 42.09% 及 62.80%。在高龄和年轻的患者中,冷 冻胚胎移植周期比例和 ICSI 比例在胚胎染色体核型异常组和正常组间差异无统计学意义。年轻组和高龄组 胚胎染色体核型异常患者的年龄 [(31.1±3.1) 岁, (39.6±2.5) 岁] 均高于染色体核型正常组 [(30.4±3.0) 岁, (37.4±2.1) 岁](P=0.018, P<0.001), 而抗苗勒管激素 (anti-Müllerian hormone, AMH)[3.68(3.80) μg/L, 2.13(2.23) μg/L] 及窦卵泡数 (13.72±7.77, 9.76±5.91) 均显著低于染色体核型正常组 [4.18(4.24) μg/L, 3.12(2.86) μg/L; 15.58±8.04, 11.56±7.29], 差异有统计学意义 (P=0.013, P=0.019; P=0.010, P=0.014)。移 植胚胎质量、移植胚胎发育类型等组间差异均无统计学意义。进一步逻辑回归分析显示,在年轻患者中, 仅血清 AMH 与自然流产胚胎染色体异常的发生密切相关 (OR=1.021, P=0.010)。纠正 AMH 后,年龄与 自然流产胚胎染色体异常的发生无相关性。而在高龄患者中,年龄与自然流产胚胎染色体异常的发生密切 相关 (OR=0.789, P=0.001)。纠正年龄后, AMH 与自然流产胚胎染色体异常的发生无相关性。结论 玻璃 化冷冻技术及 ICSI 技术不增加胚胎染色体核型异常的发生率。对于 <35 岁患者,基础 AMH 水平与胚胎 染色体核型异常密切相关。对于≥35岁患者,高龄是患者胚胎染色体核型异常的主要高危因素。

【关键词】 玻璃化冷冻技术; 卵胞质内单精子注射技术; 高龄; 抗苗勒管激素; 胚胎染色体核型基金项目: 国家重大研发项目 (2017YFC1001600); 国家自然科学基金 (81471507)

Logistic regression analysis of risk factors associated with embryo chromosomal abnormalities after embryo transfer in advanced age and young patients

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[Abstract] Objective To analyze embryo chromosomal abnormalities rate and its risk factors after assisted reproductive technology (ART) in different age groups. Methods This was a retrospective cohort study on 877 patients undergoing in vitro fertilization/intracytoplasmic sperm injection-embryo transfer (IVF/ICSI-ET) in Reproductive Medicine Center of the Sixth Affiliated Hospital of Sun Yat-Sen University between January 2016 and June 2018. All patients had embryo chromosomes tested after spontaneous abortion. Clinical data were compared between the patients with normal chromosome karyotype and those with abnormal chromosome karyotype using univariate and multivariate analysis for risk factors of abnormal chromosome karyotype in young (<35 years old) and advanced age (≥ 35 years old) patients. Results In total, 506 young and 371 advanced age patients were enrolled, whose abnormal chromosome karyotype rate was 42.09% and 62.80%, respectively. Whether young or advanced age patients, there was no statistically significant difference in the rate of freezing embryo transfer and ICSI between abnormal and normal chromosome karyotype groups. No matter young or advanced age patients, patients with abnormal chromosome karyotype were significantly older $[(31.1\pm3.1)$ years old, (39.6 ± 2.5) years old] than those with normal chromosome karyotype $[(30.4\pm3.0)$ years old, (37.4 ± 2.1) years old] (P=0.018, P<0.001), whereas anti-Müllerian hormone (AMH) [3.68(3.80) μ g/L, 2.13(2.23) μ g/L] and AFC (13.72 \pm 7.77, 9.76 ± 5.91) were significantly lower in patients with abnormal chromosome karyotype [4.18(4.24) µg/L, $3.12(2.86) \mu g/L$; 15.58 ± 8.04 , 11.56 ± 7.29] (P=0.013, P=0.019; P=0.010, P=0.014). The further logistic regression analysis confirmed that only AMH was the risk factor of abnormal chromosome karyotype in young patients (OR=1.021, P=0.010), while age was the risk factor of abnormal chromosome karyotype in advanced age patients after spontaneous abortion (OR=0.789, P=0.001). Conclusion Neither vitrified cryopreservation nor ICSI would increase incidence of abnormal chromosome karyotype. For patients younger than 35 years old, basal serum AMH was independently related to chromosomal abnormalities. For those older than 35 years old, age was the mayor risk factor for chromosomal abnormalities.

【Key words】 Vitrified cryopreservation; Intracytoplasmic sperm injection; Advanced age; Anti-Müllerian hormone; Chromosome karyotype

Fund program: National Key R&D Plan (2017YFC1001600); National Natural Science Foundation of China (81471507)

高育龄不孕妇女辅助生殖助孕前心理状况调查

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【摘要】目的 探讨高育龄不孕妇女社会学特点及进入辅助生殖助孕前心理状态。方法 本研究选择对象为 2017 年 1 月—2018 年 3 月期间于厦门大学附属第一医院生殖医学中心行辅助生殖助孕、年龄 \geqslant 35 岁的不孕症患者,共 177 例。调查问卷包括自编患者一般情况调查表、Zung 抑郁自评量表 (SDS) 以及 Zung 焦虑自评量表 (SAS),通过这些量表来评估高龄不孕患者进入辅助生殖助孕前心理状态。结果 高育龄不孕患者焦虑、抑郁发生率高。 χ^2 检验结果显示,低收入、学历高、固定职业、再婚、未生育的家庭对生育要求更加迫切,其抑郁、焦虑发生率明显增加 (P<0.05)。二项 logistic 回归分析显示,焦虑情绪的高危因素是年龄 (OR=1.178, P=0.012)、经济收入 (OR=6.706, P=0.003)、职业性质 (OR=3.624, OR=1.213, OR=0.007)、经济收入 (OR=6.436, OR=0.007)、职业性质 (OR=5.128, OR=0.013)、婚姻 (OR=1.213, OR=0.007)、共业性质 (OR=0.013)、婚姻 (OR=0.013)、婚姻 (OR=0.013)、婚姻 (OR=0.013)、婚姻 (OR=0.013)、婚姻 (OR=0.013)、相关的,是妊娠后及分娩期风险了解程度有限。在辅助生殖助孕治疗前,普遍存在焦虑和抑郁症状,尤其在高龄、固定工作、低收入、再婚、未生育等高危因素人群。应更加关注辅助生殖助孕治疗高育龄妇女的心理健康状况,加强高龄生育相关知识宣传教育。

【关键词】高龄;不孕症;辅助生殖;抑郁;焦虑

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A survey of psychological statement in advanced age infertile patients before assisted reproductive technology

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[Abstract] Objective To investigate the social characteristics and psychological status of advanced age infertile women before entering assisted reproductive technology. Methods A total of 177 infertile women aged 35 years or older planning for assisted reproductive technology in Assisted Reproductive Center of the First Affiliated Hospital of Xiamen University from January 2017 to March 2018 were included in this study. Questionnaire including editing general condition questionnaire, Zung self-rating anxiety scale (SAS) and Zung self-rating depression scale (SDS), were collected to evaluate psychological state of these patients before entering assisted reproductive technology. Results Advanced age infertile women were with high rates of anxiety and depression detection. According to χ^2 test, high income, educational background, stable work, remarriage and nullipara were more urgent requirements for children, the rates of depression and anxiety detection were significantly increased (P<0.05). The high risk factors that affect anxiety are age (QR=1.178, P=0.012), economic income (OR=6.706, P=0.003), occupation (OR=3.624, P=0.033), marital status (OR=16.065, P=0.003), and birth situation (OR=9.937, P<0.001) through binary logistic regression. The high risk factors that affect depression are age (OR=1.213, P=0.007), economic income (OR=6.436, P=0.007), occupation (OR=5.128, P=0.013), marital status (OR=15.408, P=0.005) and birth situation (OR=22.118, P<0.001) through binary logistic regression. Conclusion Infertile women are less aware of the risks of childbirth at an advanced age, especially after pregnancy and during childbirth. Before assisted reproduction technology treatment, anxiety and depression symptoms are widespread, especially with the high risks of advanced age, stable work, low income, remarried and childless. More attention should be paid to the mental health status of the advanced age infertile women who are assisted reproductive therapy, and more education should be given to the knowledge of reproduction at the old age.

[Key words] Advanced age; Infertility; Assisted reproductive technology; Depression; Anxiety

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极高龄妇女助孕的产科风险与伦理

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【摘要】随着女性年龄的增长,体外受精 (IVF) 成功率下降。即使通过辅助生殖技术 (ART) 助孕成功获得妊娠,妊娠合并症、并发症以及分娩并发症的发病风险增加,围产儿发病率和死亡率高。高龄是不良妊娠结局的独立危险因素。尤其对于极高龄女性,有循证医学高级别的证据均证实极高龄会显著增加妊娠期并发症、严重的母体并发症和胎儿/新生儿不良结局的发病风险,严重影响母婴健康,同时极高龄妇女生育也存在一系列伦理学问题。极高龄女性只有在经过严格的医学评估排除健康隐患后,方可考虑给予助孕,如年龄超过 52 岁,应拒绝给予 ART 助孕。

【关键词】 极高龄; 辅助生殖技术; 产科风险; 伦理

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Obstetric outcomes and ethical problems among women with very advanced maternal age undergoing assisted reproductive technology

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[Abstract] Advanced maternal age (AMA) was an independent risk factor that affect pregnancy outcome. With the increase of maternal age, the success rate of IVF declined. Even though AMA women conceived with assisted reproductive technology (ART), the risks for obstetric and perinatal complications significantly increased, accompanied by an increased risk of perinatal morbidity and mortality. Especially to the women with very advanced maternal age (VAMA), there was high-quality evidence verified VAMA significantly increased the risk of pregnancy complication, severe maternal complication and adverse fetal/neonatal outcomes, which seriously affected maternal and child health. Meanwhile, a series of ethical issues related to infertility treatments to women with VAMA still existed. ART could be provided to VAMA women after a thorough medical evaluation to eliminate health risks. If women over the age of 52 years, ART should be discouraged.

[Key words] Very advanced maternal age; Assisted reproductive technology; Obstetric risks; Ethics **Fund program**: National Key Research & Development Program of China (2016YFC1000206-5); National Natural Sciences Foundation of China (81571439)

高龄女性不孕症患者助孕策略

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【摘要】随着现代社会的不断发展,高龄不孕女性的数量逐渐增加,这些患者最终往往需要辅助生殖技术 (assisted reproductive technology,ART) 的帮助。然而随着女性年龄的增长,卵子数量及质量均存在不同程度的下降,如何帮助这些高龄患者尽早怀孕是辅助生殖领域一直在探讨的问题。本文对高龄女性的生理改变特点,主要为下丘脑-垂体-卵巢 (hypothalamus-pituitary-ovary,HPO) 轴的改变特点,包括高龄女性卵巢储备功能的改变与卵巢反应性评估方法、神经内分泌变化特征进行了一些探讨;同时对目前可用的控制性超促排卵 (controlled ovarian hyperstimulation,COH) 方案进行一些简单的总结和特点归纳,希望可以为每个高龄不孕女性患者寻求更好的个性化助孕策略提供参考。

【关键词】 高龄;不孕症; 助孕策略;下丘脑-垂体-卵巢轴;卵巢储备功能;控制性超促排卵DOI: 10.3760/cma.j.issn.2096-2916.2019.06.006

Strategies of assisted reproductive technology for elderly women with infertility

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[Abstract] With the continuous development of modern society, the number of elderly women with infertility is gradually increasing, and these patients often need the help of assisted reproductive technology (ART). However, with the increase of women's age, the number and the quality of eggs declines significantly. How to help these women to get pregnant as early as possible is an important issue in the field of assisted reproduction. In this article, the following topics will be discussed: 1) the characteristics of the physiological changes of elderly women about hypothalamus-pituitary-ovary (HPO) axis, including the changes in their ovarian reserve and neuroendocrine systems; 2) the summary and comparison of currently available controlled ovarian hyperstimulation (COH) protocols. It is hoped that every elderly women get optimal personalized treatment.

[Key words] Advanced age; Infertility; Strategy of treatment; Hypothalamus-pituitary-ovary axis; Ovarian reserve; Controlled ovarian hyperstimulation

高龄多囊卵巢综合征患者生育窗特点

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【摘要】多囊卵巢综合征 (polycystic ovary syndrome, PCOS) 是引起无排卵性不孕的一种常见的生殖内分泌疾病。高龄 PCOS 患者在卵巢储备和获卵数上有一定的优势,推测其生育窗延迟关闭。本文将从PCOS 患者卵子的数量和质量,以及高龄 PCOS 患者辅助生育结局三方面阐述高龄 PCOS 患者生育窗特点。

【关键词】 多囊卵巢综合征; 高龄; 生育窗; 卵巢储备; 辅助生殖技术

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Characteristics of fertile window in aged women with polycystic ovary syndrome

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[Abstract] Polycystic ovary syndrome (PCOS) is a common endocrine disorder in women of reproductive age, which affects fertility in cases of oligoanovulation. With advantages of ovarian reserve and better performance in oocyte retrieval even in late reproductive life span, one would expect women with PCOS to display a longer reproductive window. This review seeks to summarize the characteristics of fertile window in aged women with PCOS in three aspects: 1) the ovarian reserve of PCOS, 2) the oocyte quality of PCOS, 3) the clinical outcome among women undergoing assisted reproductive technology.

[Key words] Polycystic ovary syndrome; Aging; Fertile window; Ovarian reserve; Assisted reproductive technology

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黄体生成素基因多态性与拮抗剂方案中卵巢反应的临床研究

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【摘要】目的 探讨黄体生成素 β 亚基多态性 (variant-beta LH, v- β LH) 是否会影响使用 GnRH 拮抗剂方案 (gonadotropin-releasing hormone antagonist,GnRH-A) 行体外受精 (IVF) 助孕时卵巢的反应性与妊娠结局。 方法 回顾性队列研究收集 2015 年 10 月—2016 年 12 月期间在中山大学孙逸仙纪念医院生殖中心使用 GnRH-A 方案行 IVF 助孕的不孕患者 78 例,按照 v- β LH-8Arg-15Thr 位点的基因型是否发生突变分为变异型组 (n=15) 和野生型组(未发生突变,n=63),基因重组促卵泡素 (recombination follicle stimulating hormone,rFSH) 启动促排卵,观察患者的基础资料、卵泡发育速度与激素水平、IVF 相关实验室参数及妊娠结局。 结果 v- β LH 多态性的发生率为 19.23%。 LH 基因变异型与野生型不孕患者促排卵过程中的性激素变化、卵泡发育速度、r-hFSH 用量与使用时间、获卵数与可利用胚胎数等差异均无统计学意义 (P>0.05);变异型组的胚胎种植率和临床妊娠率与野生型组相似,差异均无统计学意义 (P>0.05)。结论 v- β LH 在中国女性有一定的发生率,但不影响使用 GnRH-A 方案促排卵行 IVF 助孕时的卵巢反应与妊娠结局。

【关键词】 核苷酸;基因多态性;黄体生成素;促性腺激素释放激素;体外受精基金项目:广州市科技计划产学研协同创新重大专项民生科技专题(201704020046) DOI: 10.3760/cma.j.issn.2096-2916.2019.06.008

Polymophisms of luteinizing hormone β subunit and ovarian response in gonadotropin-releasing hormone antagonist protocol for *in vitro* fertilization

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[Abstract] Objective To investigate the association between the polymorphisms of luteinizing hormone β subunit (v-βLH) with ovarian response in gonadotropin-releasing hormone antagonist (GnRH-A) protocol for *in vitro* fertilization (IVF). **Methods** A retrospective cohort study was performed. A total of 78 infertile patients with controlled ovarian hyperstimulation (COH) by the first cycle GnRH-A protocol in Sun Yat-Sen Memorial Hospital of Sun Yat-Sen University were included during October 2015 to December 2016. Patients were divided into two groups according to whether there was mutation of detection site (DNA site polymorphism of variant 8Arg-15Thr), namely wide type group (*n*=63) and variant type group (*n*=15). And recombination follicle stimulating hormone (rFSH) was used to initiate. The basic data, growth and development of follicle, hormone levels, laboratory and clinical parameters were compared between the two groups. **Results** The polymorphism incidence of v-βLH was 19.23%. No statistically significant differences of serum hormone levels, follicular development, gonadotropin (Gn) used dosages and duration, the number of oocytes retrieved and the number of available embryos were observed between the two groups. And there were no significant differences between the two groups in the implantation rate (*P*>0.05) and the clinical pregnancy rate (*P*>0.05). **Conclusion** There was a certain incidence of v-βLH in China. However, it did not affect the ovarian response and pregnancy outcome when patients were treated with GnRH-A protocol for IVF.

Key words Nucleotides; Polymorphism genetic; Luteinizing hormone; Gonadotropin-releasing hormone; Fertilization *in vitro*

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微刺激促排卵方案中未获卵周期预测因素的探讨

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【摘要】目的 探讨微刺激促排卵方案中预测获卵失败发生的临床因素。方法 回顾性分析 2016 年8月—2018 年4月就诊于上海永远幸妇科医院生殖医学中心接受微刺激促排卵周期 846 个,其中获卵失败周期 97 个。对同时具有获卵失败周期 (56 个,获卵失败组)和获卵成功周期 (77 个,获卵成功组)的 50 名患者的临床资料进行自身对照分析。结果 同一患者在不同促排卵周期基础内分泌水平差异无统计学意义,第8日、第9~10日及扳机日血清雌二醇水平在获卵成功组比获卵失败组增长较快,差异有统计学意义 [(233.33±134.92) ng/L 比 (176.82±100.68) ng/L,P=0.011,(525.40±293.88) ng/L比 (397.02±214.58) ng/L,P=0.034,(690.48±347.36) ng/L 比 (564.85±296.72) ng/L,P=0.030]。第8日血清卵泡刺激素 (FSH)水平在获卵失败周期中升高明显 [(16.91±9.28) IU/L 比 (13.74±5.77) IU/L,P=0.039]。结论 在微刺激治疗中,治疗周期中雌激素水平持续偏低、第8日血清 FSH 水平增高,应警惕本周期获卵失败风险的增加。

【关键词】辅助生殖技术; 克罗米酚; 获卵; 雌激素

Research on related features of oocytes retrieval failure in mild stimulation protocol

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[Abstract] Objective To analyze the related factors on oocytes retrieval failure in mild stimulation protocol. Methods There were 97 cycles with oocyte retrieval failure from 846 treatment cycles in mild stimulation protocol. Among these patients, 50 women who had another cycle with successful oocyte retrieval were retrospectively analyzed. Results Estrogen levels on day 8, day 9–10 and trigger day were significantly higher in the cycles of successful oocyte retrieval than those in the cycle of oocyte retrieval failure $[(233.33\pm134.92) \text{ ng/L } vs. (176.82\pm100.68) \text{ ng/L}, P=0.011; (525.40\pm293.88) \text{ ng/L } vs. (397.02\pm214.58) \text{ ng/L}, P=0.034; (690.48\pm347.36) \text{ ng/L } vs. (564.85\pm296.72) \text{ ng/L}, P=0.030]. Follicle stimulating hormone (FSH) levels on day 8 increased significantly in oocyte retrieval failure cycle than in successful oocyte retrieval cycles <math>[16.91\pm9.28) \text{ IU/L } vs. (13.74\pm5.77) \text{ IU/L}, P=0.039].$ Conclusion Patients with consistent lower levels of estrogen during the cycle and higher level of FSH on day 8 would have higher chance of oocyte retrieval failure in mild stimulation protocol.

[Key words] Reproductive technique, assisted; Clomiphene citrate; Oocyte retrieval; Estrogens DOI: 10.3760/cma.j.issn.2096-2916.2019.06.009

•实验研究•

内脏脂肪介导中年雌性大鼠黄体生成素高峰分泌异常的研究

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【摘要】目的 研究增龄性内脏脂肪增加可能通过中枢机制介导黄体生成素(LH)分泌异常,探索早 期女性生殖衰老发生的相关因素及干预策略。方法 阴道涂片法筛选性周期规律的 36 只中年 (9~11 个月) 雌性 Sprage-Dawley 大鼠,随机分为减除内脏脂肪 (visceral fat removal, VFR) 组和假手术组,VFR 组大鼠 经腹部手术移除内脏(包括卵巢及子宫、肾周及膀胱周围)脂肪,假手术组大鼠于腹部正中切口暴露脏器 后即刻缝合。3周后所有大鼠均接受去卵巢手术,术后1周给予外源性激素注射模拟雌激素正反馈。观 察并比较大鼠体质量、体脂百分比及葡萄糖耐受情况;经颈静脉插管连续取血测定 LH 分泌水平;免疫 组织化学双标记检测下丘脑促性腺激素释放激素 (GnRH) 神经元表达 c-Fos 的百分数; 荧光定量 PCR 检 测下丘脑前脑 Igf1、Igf1r、Kiss1、Kiss1r、Nr1、Nr2b、Slc17a6 和 Slc32a1 的 mRNA 表达。结果 内脏 脂肪移除术后 4 周, VFR 组大鼠外源性激素诱导的总 LH 分泌量 [(4 658.0±1 312.0) µg/L] 及 LH 分泌高 峰 [(16.0±4.5) μg/L] 明显高于假手术组 [(1 906.0±241.1) μg/L; P=0.04; (6.1±0.7) μg/L, P=0.03]; 下丘脑 GnRH 神经元表达 c-Fos 百分数 (53.9%±4.2%) 较假手术组增加了 1.4 倍 (36.2%±5.9%, P=0.01); 与术前 基线数值相比,大鼠的体质量、体脂百分数及葡萄糖耐受在内脏脂肪移除术后差异无统计学意义 (P>0.05); 内脏脂肪移除不改变下丘脑前脑 Igf1、Igf1r、Kiss1、Kiss1r、Nr1、Nr2b、Slc17a6 和 Slc32a1 的 mRNA 表达。 结论 减少内脏脂肪显著增加中年雌性大鼠外源性激素诱导 LH 高峰分泌及下丘脑 GnRH 神经元的激活, 提示内脏脂肪可能通过中枢调控机制影响雌激素正反馈作用介导女性生殖衰老的发生,减少内脏脂肪可能 有助于改善早期生殖衰老的特征表型。

【关键词】 衰老;内脏脂肪;雌激素;促性腺激素释放激素;黄体生成素

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•实验研究•

Intra-abdominal visceral fat mediates the ovarian-steroid-induced luteinizing hormone surge dysfunction in middle-aged female rats

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[Abstract] Objective To investigate central mechanisms of age-related increased abdominal visceral fat and luteinizing hormone (LH) surge dysfunction in middle-aged females and explore possible intervention strategies for female reproductive aging. **Methods** Thirty-six cycling middle-aged Sprage-Dawley rats were selected by vaginal smears and randomly assigned to sham surgery or intra-abdominal/pelvic adipectomy (visceral fat removal, VFR) group. A mid-ventral abdominal incision cut was provided for VFR and sham rats, intra-abdominal visceral fat (including the gonad, perivesical and perinephric fat pads) was bilaterally excised for VFR rats but organs were exteriorized and placed back into abdominal cavity before skin closed for sham controls. Rats were allowed to recover for three weeks before they were gonadectomized (OVX). One week after OVX, estradiol and progesterone were primed to induce a LH surge. Serial blood sampling by jugular vein catheterization was used to assess the onset and magnitude of the LH surge, body weight and composition and glucose tolerance were determined as well. To quantify GnRH neuronal activation, as determined by c-Fos co-expression, rats were perfused and performed with immunohistochemistry. Real-time PCR was used to quantify hypothalamic neurotransmitters gene expression known to change with aging including Igf1, Igf1r, Kiss1, Kiss1r, Nr1, Nr2b, Slc17a6 and Slc32a1. Results Rats in VFR group exhibited a significant elevation of peak $[(16\pm4.5) \,\mu\text{g/L}]$ and total LH release $[(4658.0\pm1312.0) \,\mu\text{g/L}]$ and 1.4-fold increase of GnRH neuronal activation (53.9% \pm 4.2%) compared with sham operated females [(6.1 \pm 0.7) μ g/L, P=0.03; $(1\ 906.0\pm241.1)\ \mu g/L$, P=0.04; 36.2 ± 5.9 , P=0.01]. However, no significant difference in glucose tolerance, body weight or body composition was found for VFR or sham females when compared with their baseline values obtained before surgery. VFR did not change neurotransmitters gene expression in the anterior hypothalamus when compared with sham females. Conclusion Intra-abdominal visceral fat removal markedly increased ovariansteroids-induced LH surge and GnRH neuronal activation in middle-aged females, this study suggests that increased intra-abdominal visceral fat in middle-aged females may contribute to female reproductive aging through adversely affects estradiol positive feedback action on the hypothalamus.

Key words Aging; Intra-abdominal visceral fat; Estradiol; Gonadotropin-releasing hormone; Luteinizing hormone

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·现场报道 ·

人工流产女性伴侣生殖健康知信行现状及 影响因素

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【摘要】目的 研究人工流产女性伴侣生殖健康知信行的现状及其影响因素,为促进男性参与生殖健康相应措施的制定提供参考依据。方法 本研究于 2016 年 8 月—10 月期间采用分层随机抽样法抽取长沙市 3 家医院,共 382 名陪同女性手术的女性伴侣作为研究对象。通过自编问卷调查意外妊娠原因和人工流产女性伴侣生殖健康知信行现状。 结果 58.36%的人工流产源于避孕失败,35.01%因未采取避孕措施;性伴侣参与生殖健康知信行总得分为(163.32±15.53)分,其中知识得分(58.89±6.67)分,态度得分(65.09±7.56)分,行为得分(39.35±5.94)分;单因素方差分析结果显示,不同年龄、文化程度、个人月收入、家庭人均月收入、伴侣文化程度、父母感情状况、与伴侣感情状况、共生育子女数在人流女性伴侣参与生殖健康总得分上差异有统计学意义(P<0.05)。结论 人工流产女性伴侣参与生殖健康的态度较为积极,但是生殖健康的知识水平有待提高,行为有待改善,尤其是避孕知识及行为,相应措施的制定可参考上述影响因素。

【关键词】 人工流产;伴侣;参与生殖健康;知信行;影响因素

·现场报道。

Present situation and determinants of knowledge-attitude-practice of reproductive health in induced abortion female's partners

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[Abstract] Objective To analyze the current status and determinants of knowledge-attitude-practice (KAP) of reproductive health in induced abortion female's partners and to provide scientific evidence to improve the male's participation in the reproductive health. Methods This research selected 382 induced abortion female's partners who accompanied the female to the hospital from 3 hospitals in Changsha as the respondents by stratified random sampling method during August to October in 2016. Self-designed questionnaires were used to investigate the causes of unexpected pregnancy and current status of KAP of reproductive health in induced abortion female's partners. Results
The induced abortion was caused by accidental pregnancy, which 58.36% was due to contraceptive failure, while 35.01% was due to unprotected sex; the overall average score of Reproductive Health KAP among induced abortion female's partners was 163.32 ± 15.53, the average score of knowledge was 58.89 ± 6.67 , the average score of attitude was 65.09 ± 7.56 , the average score of behavior was 39.35 ± 5.94. ANOVA analysis showed that the age, the degree of education, personal monthly income, family average monthly income, the partner's degree of education, the relationship status of parents, the relationship status with the partner and the number of children had significant differences on the overall KAP score of reproductive health in the induced abortion female's partners (P<0.05). Conclusion The attitude to reproductive health of the induced abortion female's partners was relatively positive. However, the level of knowledge and practice required improvement, especially for the contraception. The methods that aimed to improve the situation could be made based on these factors.

Key words Induced abortion; Partner; Participation in reproductive health; Knowledge-attitude-behavior; Determinants

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·临床报道 ·

促性腺激素释放激素拮抗剂方案改善助孕反复失败的卵巢低反应患者胚胎质量及体外受精结局的自身对照研究

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【摘要】目的 探讨促性腺激素释放激素激动剂 (GnRH-a) 长方案助孕的卵巢低反应 (POR) 患者失败后改用促性腺激素释放激素拮抗剂 (GnRH-A) 方案促排卵对胚胎质量及体外受精 (IVF) 结局的改善效果。方法 回顾性分析 2017 年 2 月—2018 年 2 月期间在兰州大学第一医院生殖医学专科医院 53 例 POR 患者 GnRH-a 长方案助孕失败后改用 GnRH-A 方案的前后自身对照研究,比较两种方案的促性腺激素 (Gn) 使用间、Gn 使用总量、hCG 注射日雌二醇、hCG 注射日黄体生成素 (LH)、hCG 注射日孕酮、hCG 注射日子宫内膜厚度、获卵数、受精率、卵裂率、可移植胚胎数、优质胚胎率、移植胚胎数、移植日子宫内膜厚度、种植率、周期取消率,计算 GnRH-A 组的临床妊娠率。结果 GnRH-A 组的 Gn 使用时间 [(11.3±3.4) d]、Gn 使用总量 [(2 827.6±427.4) IU]、hCG 注射日 LH[(1.24±0.76) IU/L]、周期取消率 (5.66%) 与 GnRH-A 长方案组 [(13.7±3.7) d, P<0.001;(3 824.8±682.4) IU, P=0.037;(3.12±2.21) IU/L, P<0.001;7.55%,P=0.027] 相比均显著下降;获卵数 (4.4±2.1)、优质胚胎率 (45.98%)、种植率 (31.55%) 与 GnRH-a 长方案组 (3.4±2.0, P=0.035;40.23%, P=0.031;27.45%, P=0.041) 相比均显著增加;而 hCG 注射日雌二醇、hCG 注射日孕酮、hCG 注射日子宫内膜厚度、受精率、卵裂率、可移植胚胎数、移植胚胎数、移植日子宫内膜厚度组间差异均无统计学意义 (P>0.05);GnRH-A 组的临床妊娠率为 32.00%。结论 POR 患者采用 GnRH-a 长方案助孕失败后应用 GnRH-A 方案促排卵有助于改善胚胎质量及 IVF 结局。

【关键词】促性腺激素释放激素拮抗剂;卵巢低反应;胚胎质量;受精,体外;自身对照研究DOI: 10.3760/cma.j.issn.2096-2916.2019.06.012

·临床报道·

Gonadotropin-releasing hormone antagonist protocol improves embryo quality and *in vitro* fertilization outcomes in poor ovarian response patients with repeated *in vitro* fertilization failure: a self-controlled study

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[Abstract] Objective To discuss the effect of gonadotropin-releasing hormone antagonist (GnRH-A) protocol on the improvement of embryo quality and pregnancy outcome after the pregnancy failure of gonadotropin-releasing hormone agonist (GnRH-a) protocol performed for the poor ovarian response (POR) patients who suffered repeated in vitro fertilization (IVF) failure accompanied by poor embryo quality. Methods A selfcontrolled study was carried out retrospectively to analyze 53 POR patients who switch to GnRH-A protocol after the pregnancy failure performed by the GnRH-a protocol in the Reproductive Medicine Special Hospital of the 1st Hospital of Lanzhou University from February 2017 to February 2018. The duration of gonadotropin (Gn) used, total dosage of Gn used, the levels of estradiol, luteinizing hormone (LH) and progesterone on the day of hCG injection, endometrial thickness on the day of hCG injection, No. of oocytes retrieved, fertilization rate, cleavage rate, No. of embryos obtained for embryo transfer, rate of high-quality embryos, No. of embryos transferred, endometrial thickness on the day of embryo transfer, implantation rate, cancelling rate between GnRH-A and GnRH-a groups were compared, and the clinical pregnancy rate of GnRH-A group was also calculated. **Results** The duration of Gn used $[(11.3\pm3.4) \text{ d}]$, total dosage of Gn used [(2 827.6 ± 427.4) IU], LH level on the day of hCG injection [(1.24 ± 0.76) IU/L], cancelling rate (5.66%) of GnRH-A group were significantly lower than those of GnRH-a group [(13.7±3.7) d, P<0.001; (3 824.8±682.4) IU, P=0.037; (3.12±2.21) IU/L, P<0.001; 7.55%, P=0.027]. No. of oocytes retrieved (4.4 ± 2.1), rate of high-quality embryos (45.98%), implantation rate (31.55%) of GnRH-A group were significantly higher than those of GnRH-a group $(3.4 \pm 2.0, P=0.035; 40.23\%, P=0.031; 27.45\%, P=0.041)$. There were no significant differences in the estradiol and progesterone on the day of hCG injection, endometrial thickness on the day of hCG injection, fertilization rate, cleavage rate, No. of embryos obtained for embryo transfer, No. of embryos transferred, endometrial thickness on the day of embryo transfer between the two groups (P>0.05). And the clinical pregnancy rate of GnRH-A group was 32.00%. Conclusion The GnRH-A protocol may help to improve embryo quality and IVF outcomes for POR patients after the pregnancy failure performed by the GnRH-a protocol.

(Key words) Gonadotropin-releasing hormone antagonist; Poor ovarian response; Embryo quality; Fertilization *in vitro*; Self-controlled study

·临床报道 ·

8例创伤性子宫动静脉瘘患者血流动力学特征探讨

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【摘要】目的 探讨经阴道超声诊断创伤性子宫动静脉瘘的价值。方法 对同济大学附属上海第一妇婴保健院 2015—2018 年间 28 例宫内操作后超声拟诊为子宫动静脉瘘的患者进行回顾性分析。根据诊断结果将其分为动静脉瘘组和残留组。比较两组病灶部位血流动力学参数收缩期峰值流速 (PSV)、舒张期末峰值流速 (EDV)、收缩 / 舒张比值 (S/D)、搏动指数 (PI)、阻力指数 (RI),并进行统计学分析。结果 经手术病理或数字剪影血管造影术 (DSA) 证实为子宫动静脉瘘者 8 例,流产后残留者 15 例,失访 5 例。动静脉瘘组 S/D(1.41±0.10)、PI(0.33±0.05)、RI (0.30±0.05) 值均低于残留组 S/D(1.74±0.24)、PI(0.52±0.09)、RI(0.41±0.08),差异有统计学意义 (P 均 <0.01)。而动静脉瘘组 PSV(53.21±22.99) 及 EDV(37.05±15.72)与残留组 PSV(53.11±19.80) 及 EDV(30.59±11.78) 变化幅度均较大,组间比较差异均无统计学意义 (P 均 >0.05)。结论 经阴道超声测量病灶部位血流动力学参数变化有助于提高子宫动静脉瘘诊断准确性。

【关键词】子宫动静脉瘘; 创伤性; 不全流产; 多普勒; 超声

·临床报道 ·

Characteristics of hemodynamic changes in 8 cases of uterine arteriovenous malformation patients

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[Abstract] Objective To study the value of transvaginal ultrasound in diagnosis of traumatic uterine arteriovenous malformation. **Methods** A retrospective analysis was conducted on 28 cases of uterine arteriovenous malformation diagnosed by ultrasound after intrauterine operation in Shanghai First Maternity and Infant Hospital, Tongji University School of Medicine from 2015 to 2018. According to the diagnosis results, they were divided into arteriovenous malformation group and residual group. Peak systolic velocity (PSV), end diastolic velocity (EDV), systolic/diastolic ratio (S/D), pulsatility index (PI) and resistive index (RI) were compared. **Results** Eight cases were confirmed as uterine arteriovenous malformation by pathology or digital silhouette angiography (DSA), 15 cases were abortion incomplete, and 5 cases were lost to follow-up. S/D (1.41 \pm 0.10), PI (0.33 \pm 0.05), RI (0.30 \pm 0.05) in uterine arteriovenous malformation group were significantly lower than those in residue group (1.74 \pm 0.24, 0.52 \pm 0.09, 0.41 \pm 0.08)(P<0.01). The changes of PSV and EDV were not statistically different. **Conclusion** The hemodynamic parameters of the focus by transvaginal ultrasound can improve the accuracy of traumatic uterine arteriovenous malformation.

[Key words] Uterine arteriovenous malformation; Traumatic; Post-abortion residue; Doppler; Ultrasonography

3D 打印技术在生殖医学中的应用

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【摘要】3D打印是一种新兴的快速、高效、低成本的制造手段,以三维数字模型结合逐层打印的方式将材料构筑成既定模型的技术。目前,3D打印已成为再生医学中重要的技术手段,在骨科、口腔、眼科等医学领域中得到广泛应用。现亦有研究报道,3D打印技术也逐步应用于生殖领域,如打印卵巢、精子、子宫附件以及在生殖过程中起重要作用的乳腺、胚胎干细胞等,成为生殖医学领域的崭新热点。本文总结了3D打印技术在生殖医学中的应用现状,并展望其应用前景。

【关键词】 3D 打印技术; 生殖系统; 应用; 前景

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Application of three dimensiona printing technology in reproductive medicine

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[Abstract] Three dimensiona (3D) printing technology, a three-dimensional digital model combined with layer-by-layer printing to build materials into established models, is already recognized as a new fast, efficient and low-cost manufacturing method. Nowadays, 3D printing has been applied in tissue engineering and regenerative medicine, including the orthopaedics, oral cavity, ophthalmology and other medical fields. Moreover, a few researches and applications reported the application of 3D printing technology in the print of reproductive fileds, such as printed ovary, sperm, adnexa uteri and breast, human embryonic stem cells which have an important in the reproductive process. In this study, we analyze the 3D printing current application in reproductive medicine, and propose forecast in the future.

Key words Three dimensional printing; Reproductive system; Application; Prospect

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卵巢低反应患者促排卵方案的研究进展

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【 摘要 】 卵 巢 低 反 应 (poor ovarian response, POR) 即 在 控 制 性 超 促 排 卵 (controlled ovarian hyperstimulation, COH) 中卵巢对外源性促性腺素 (gonadotropins, Gn) 刺激反应不良的状态,主要表现为获卵数少,周期取消率高,且临床妊娠率低。对于 POR 患者有长方案、短方案、超短方案、拮抗剂方案、自然周期、卵泡期及黄体期促排卵等多种促排卵方案可供选择,但是选择何种方案能获得更多更好的卵母细胞及优质胚胎,降低周期取消率,改善其助孕结局是辅助生殖技术 (assisted reproductive technology, ART) 的难点之一,也是困扰临床医生的一大难题。本文就目前临床应用于 POR 患者的促排卵方案进行讨论分析。

【关键词】 卵巢低反应; 控制性超促排卵; 临床结局 DOI: 10.3760/cma.j.issn.2096-2916.2019.06.015

Research progress of ovarian stimulation regimens in patients with poor ovarian response

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[Abstract] Poor ovarian response (POR) is a status of decreased ovarian reservation to the exogenous gonadotropins (Gn) in controlled ovarian hyperstimulation (COH). The main manifestations are low number of oocytes retrieved, high rate of cycle cancellation, and low clinical pregnancy. For POR patients, there are a variety of ovarian stimulation regimens such as long protocol, short protocol, ultra-short protocol, antagonist protocol, natural-cycle, follicular and luteal phase ovulation, but which option can be used to obtain more good oocytes and high-quality embryos, reducie the cycle cancellation rate and improve their pregnancy outcomes is one of the difficulties of assisted reproductive technology (ART), and it is also a major problem that plagues clinicians. This article discusses the current ovulation stimulation regimens for clinical application in POR patients.

[Key words] Poor ovarian response; Controlled ovarian hyperstimulation; Clinical outcome DOI: 10.3760/cma.j.issn.2096-2916.2019.06.015

宫腔灌注改善子宫内膜容受性的研究进展

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【摘要】子宫内膜容受性是胚胎种植的关键,但目前针对子宫内膜容受性尚无公认有效的改善方法。宫腔灌注是当今较新的一种治疗方法,本文通过回顾文献,以宫腔灌注药物为分类,介绍治疗方法,分析作用机制、评判疗效及前景,对宫腔灌注的最新研究进展进行总结。虽然大部分文献表明宫腔灌注可以有效提高子宫内膜容受性,但仍需要更多高质量临床研究证明其有效性,同时也亟需制定规范的诊疗方案与适应证。

【关键词】 胚胎植入; 辅助生殖技术; 子宫内膜容受性; 宫腔灌注

Advanced progress of intrauterine perfusion in improving endometrial receptivity

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【Abstract】 Endometrial receptivity is the key to embryo implantation, but there is no recognized effective treatment for patients to improving endometrial receptivity. Nowadays, intrauterine perfusion is a new treatment. Based on reviewing the literature, this paper classifies the drugs of intrauterine perfusion, introduces the treatment approaches, analyzes the mechanism of action, evaluates the curative effect and prospects to summarize the advanced progress of intrauterine perfusion. Although the majority of studies demonstrated that intrauterine perfusion can effectively improve endometrial receptivity, it still needs more high-quality clinical studies to prove their effectiveness. And there is also an urgent need to develop standardized diagnosis and treatment programs, and probe into indication.

[Key words] Embryo implantation; Reproductive technology, assisted; Endometrial receptivity; Intrauterine perfusion

钙敏感受体与女性生殖系统关系的研究进展

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【摘要】 钙敏感受体 (CaSR) 是 G 蛋白耦联受体的 C 家族成员,可感应细胞外的 Ca^{2+} 浓度。CaSR 通过结合 Ca^{2+} 而激活多种细胞内途径,在维持机体钙稳态中起到重要作用,与某些女性生殖系统疾病的发生、发展过程有一定的关系。本文主要综述了 CaSR 与女性生殖系统疾病的关系。

【关键词】 钙敏感受体; Ca²⁺; 女性; 生殖系统

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Research progress of the relationship between calcium-sensing receptor and female reproductive system

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[Abstract] Calcium sensing receptor (CaSR) is a G-protein coupled receptor which senses extracellular calcium. CaSR plays an important role in maintaining the calcium homeostasis of the body by combining calcium ions and activating avarious intracellular patways, and may be related to the occurrence and development of certain diseases of the female reproductive system. In the present study, we mainly summarized the role of CaSR in the female reproductive system diseases.

[Key words] Calcium sensing receptor; Ca²⁺; Female; Reproductive system

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母 - 胎界面中巨噬细胞与精氨酸代谢途径关系的研究进展

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【摘要】母-胎界面中,巨噬细胞占全部免疫细胞的 20%,其在妊娠的各个时期都发挥着重要作用,如子宫内膜和血管的重塑过程、滋养层细胞的侵袭、胚胎的免疫耐受以及最终的分娩。精氨酸途径参与了很多的代谢过程,而巨噬细胞中的精氨酸途径主要包括两条途径:①精氨酸在一氧化氮合酶 (NOS) 的作用生成 NO 和瓜氨酸 (NO 途径);②精氨酸在精氨酸酶的作用下生成鸟氨酸和尿素(鸟氨酸途径)。本文主要对近年来母-胎界面中巨噬细胞与精氨酸代谢途径关系进行回顾和展望。

【关键词】精氨酸;巨噬细胞;母-胎界面

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Progress on the role of arginine pathway in macrophages at the maternal-fetal interface

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[Abstract] In the maternal-fetal interface, macrophages, 20% of all immune cells, which play an important role in various periods of pregnancy, such as endometrial and vascular remodeling, invasion of trophoblast cells, the immune tolerance of embryo, and the final delivery. The arginine pathway is involved in many metabolic processes, and the arginine pathway in macrophages mainly involves two pathways: 1) the action of arginine nitric oxide synthase (NOS) to produce NO and citrulline (NO pathway); 2) Arginine produces ornithine and urea (ornithine pathway) under the action of arginase. This article focuses on the recent review of the maternal-fetal interface of arginine metabolic pathways and macrophages.

Key words Arginine; Macrophages; Maternal-fetal interface

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