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中国男性生育力保存专家共识

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【摘要】 男性生育力保存 (male fertility preservation , MFP) 是应对男性不育的重要策略,目的是为有需求的男性提供生育力保存,为男性在实施影响生育诊断与治疗前或暴露前保存生育力,为在未来生育时提供可用精子。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发起,并组织 MFP 领域的专家成立编写组后撰写。内容涉及 MFP 的各个方面,包括 MFP 的适用人群、MFP 前的准备、不同样本获取的方法及具体冻融方法、冻存样本保存方法以及 MFP 相关的质量控制与伦理问题等。本共识重视规范 MFP 的应用范围,同时聚焦精子冷冻、复苏过程及质量控制,为从事生殖医学、男科学、妇产科学或肿瘤生育力保存的专业医务人员,尤其为辅助生殖机构和人类精子库的专业人员提供专家咨询建议。

【关键词】 男性生育力保存; 精子冷冻; 肿瘤; 生殖技术,辅助; 人类精子库

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Chinese consensus on male fertility preservation

Chinese Male Fertility Preservation Consensus Writing Committee

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【Abstract】 Male fertility preservation (MFP) refers the technique that provides sperm for meeting the demand in the future by preserving male fertility before treatment or exposure that affects fertility. MFP is an important strategy to deal with male infertility. The present consensus was initiated by the Reproductive Andrology Group of the Chinese Association of Reproductive Medicine, and written by a consensus committee made up of MFP specialists. It covered various aspects of MFP, including the applicable population of MFP, preparation prior to MFP, sample retrieval methods and specific frozen-thawed methods, frozen sample preservation protocol, quality control and ethical issues related to MFP. This consensus will provide expert advice to medical professionals engaged in reproductive medicine, andrology, obstetrics and gynecology, or oncology fertility preservation, especially to professionals in assisted reproductive institutions and human sperm banks.

【Key words】 Male fertility preservation; Sperm cryopreservation; Tumour; Reproductive technology, assisted; Human sperm bank

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卵泡期长效长方案在符合卵巢高反应预测指标患者中的运用及其发生高反应的危险因素分析

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【摘要】 目的 分析卵泡期长效长方案在符合卵巢高反应预测指标患者中的运用及高反应发生的危险因素。方法 运用病例对照研究方法, 回顾性分析 2016 年 1 月 1 日至 2019 年 6 月 1 日期间于福建省妇幼保健院生殖中心就诊的符合卵巢高反应预测指标的 664 例患者的临床资料。通过 logistic 回归, 筛选卵巢高反应的独立危险因素。运用受试者工作特征曲线下面积 (area under the curve, AUC) 评估所筛选各卵巢高反应独立危险因素的预测准确度。结果 664 例患者中 10 例 (1.51%) 发生卵巢低反应, 356 例患者 (53.61%) 取得正常的卵巢反应, 298 例患者 (44.88%) 发生高反应。正常反应组的中重度卵巢过度刺激综合征发生率 [3.09% (11/356)] 显著低于高反应组 [8.39% (25/298)], $P=0.003$; 每移植周期临床妊娠率与高反应组间差异无统计学意义 ($P>0.05$); 高反应组流产率为正常反应组的 2 倍多, 但差异无统计学意义 ($P>0.05$)。多因素 logistic 回归提示人绒毛膜促性腺激素 (human chorionic gonadotropin, hCG) 注射日黄体生成素 (luteinizing hormone, LH) 水平与卵巢高反应的发生呈显著负相关。hCG 注射日 LH 水平预测卵巢高反应发生的 AUC 为 0.594, hCG 注射日 LH 水平 ≤ 1.0 IU/L 是高反应发生的独立危险因素。结论 卵泡期长效长方案运用于符合卵巢高反应预测指标的患者可获得较为理想的临床结局。控制性卵巢刺激过程中适当添加外源性 LH 可能有助于减少卵巢高反应的发生。

【关键词】 卵巢刺激; 黄体生成素; 卵泡期长效长方案; 卵巢高反应

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Clinical outcomes of long agonist protocol in predicted hyper responders and the risk factors associated with hyper ovarian response

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【 Abstract 】 Objectives To investigate the clinical outcomes of long agonist protocol in predicted hyper responders, and to explore the risk factors associated with hyper ovarian response in these patients. **Methods** In this retrospective case-control study, 664 predicted hyper responders were included. All patients were from Reproductive Center of Fujian Maternity and Child Health Hospital, and were in treatment during January 1, 2016 and June 1, 2019. Logistic regression was applied to screen out the independent risk factors of hyper ovarian response. The prediction accuracy of the independent risk factors was evaluated by calculating the area under the receiver operating characteristic curve (AUC). **Results** Totally 10 (1.51%) of all patients occurred poor ovarian response, 356 (53.61%) of all patients achieved normal ovarian response, and 298 (44.88%) of them got hyper ovarian response. The rate of moderate-to-severe ovarian hyperstimulation syndrome (OHSS) from normal response group [3.09% (11/356)] was significantly lower than that from hyper response group [8.39% (25/298), $P=0.003$]. The rate of clinical pregnancy per transfer showed no statistical significance between the two groups ($P>0.05$). The miscarriage rate was more than two times in normal response group compared with high response group, but without statistical significance ($P>0.05$). Multivariate logistic regression analysis showed that luteinizing hormone (LH) level on human chorionic gonadotropin (hCG) injection day was negatively correlated with the occurrence of hyper ovarian response. The AUC of LH level on hCG injection day was 0.594. LH level on hCG injection day ≤ 1.0 IU/L was an independent risk factor of hyper ovarian response. **Conclusion** Long agonist protocol is a good option for predicted hyper responders. LH supplementation might be helpful in controlled ovarian stimulation to reduce the incidence of hyper ovarian response.

【 Key words 】 Ovarian stimulation; Luteinizing hormone; Long agonist protocol; Hyper ovarian response

Fund program: Fujian Provincial Health Technology Project (2019-ZQN-22); Fujian Provincial Natural Science Foundation (2019J05137); National Key R&D Program of China (2018YFC1002105)

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低抗苗勒管激素女性行体外受精- 胚胎移植累积分娩率及其影响因素 探讨

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【摘要】 目的 探讨抗苗勒管激素 (anti-Müllerian hormone, AMH) ≤ 1 $\mu\text{g/L}$ 的女性行体外受精-胚胎移植 (*in vitro* fertilization and embryo transfer, IVF-ET) 助孕的累积分娩率及其影响因素。方法 回顾性队列研究分析 2016 年 7 月至 2018 年 2 月期间在河南省人民医院生殖医学中心首次接受 IVF-ET 助孕治疗的 793 例 AMH ≤ 1 $\mu\text{g/L}$ 不孕女性的临床资料, 根据每促排卵周期最终是否获得活胎分娩分为累积分娩组和未获得分娩组, 比较两组间的一般情况, logistic 回归分析影响累积分娩率的因素, 并对不同年龄段的临床结局进行比较。结果 ①每起始周期累积分娩率为 23.83% (189/793)。累积分娩组和未获得分娩组间患者年龄 [33 (30, 37) 岁比 39 (34, 43) 岁]、AMH [0.67 (0.46, 0.87) $\mu\text{g/L}$ 比 0.51 (0.22, 0.74) $\mu\text{g/L}$]、窦卵泡计数 (antral follicle count, AFC) [6 (4, 8) 比 4 (2, 6)]、基础卵泡刺激素 (basal follicle-stimulating hormone, bFSH) [9.11 (6.98, 11.03) IU/L 比 11.06 (7.75, 13.13) IU/L]、促性腺激素 (gonadotropin, Gn) 起始用量 [225.0 (187.5, 225.0) IU 比 225.0 (225.0, 300.0) IU]、Gn 使用总量 [2 475.0 (1 800.0, 3 137.5) IU 比 2 100.0 (1 575.0, 2 850.0) IU]、Gn 使用时间 [10 (8, 12) d 比 9 (6, 11) d]、获卵数 [5.0 (3.0, 7.5) 枚比 2.5 (1.0, 4.0) 枚]、 M_{II} 卵数 [4 (3, 6) 枚比 2 (1, 3) 枚] 及卵裂期可移植胚胎数 [3.0 (2.0, 4.5) 枚比 1.0 (0, 2.0) 枚] 差异均有统计学意义 (P 均 < 0.001)。②多因素 logistic 回归分析显示, 年龄 ($OR=0.878$, 95% $CI=0.846\sim 0.911$, $P<0.001$) 是累积分娩率的独立影响因素。对不同年龄段的分组分析显示, 随着年龄的增加, 每起始周期累积妊娠率及累积分娩率显著下降 (P 均 < 0.001), 当年龄 > 40 岁后无可利用胚胎周期取消率显著增高 ($P<0.001$)。结论 年龄是影响低 AMH 女性行 IVF 助孕累积分娩率的显著因素, 累积分娩率随着年龄的增加逐渐降低。

【关键词】 抗苗勒管激素; 累积分娩率; 受精, 体外; 胚胎移植

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Cumulative delivery rate and related factors of infertile women with low anti-Müllerian hormone level during *in vitro* fertilization and embryo transfer treatment

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【 Abstract 】 Objective To explore the cumulative delivery rate and related factors of infertile women with anti-Müllerian hormone (AMH) no more than 1 µg/L during *in vitro* fertilization and embryo transfer (IVF-ET) treatment. **Methods** In this retrospective cohort study, we analyzed 793 infertile women with AMH no more than 1 µg/L and underwent their first IVF-ET treatment in Henan Provincial People's Hospital between July 2016 and February 2018. All the patients were categorized into two groups according to cumulative delivery with at least one live baby or not. Baseline data and outcomes were compared between the two groups. The regression analysis was conducted to identify the independent factors of cumulative delivery rate and clinical outcomes of different age groups were compared. **Results** 1) The total cumulative delivery rate per start cycle was 23.83% (189/793). There were significant differences in age [33(30,37) years vs. 39(34,43) years], AMH [0.67(0.46,0.87) µg/L vs. 0.51(0.22,0.74) µg/L], antral follicle count (AFC) [6(4,8) vs. 4(2,6)], basal follicle-stimulating hormone (bFSH) [9.11(6.98,11.03) IU/L vs. 11.06(7.75,13.13) IU/L], starting dosage of gonadotropin (Gn) used [225.0(187.5,225.0) IU vs. 225.0(225.0,300.0) IU], total dosage of Gn used [2 475.0(1 800.0,3 137.5) IU vs. 2 100.0(1 575.0,2 850.0) IU], duration of Gn stimulation [10(8,12) d vs. 9(6,11) d], number of oocytes retrieved [5.0(3.0,7.5) vs. 2.5(1.0,4.0)], number of M_{II} oocytes [4(3,6) vs. 2(1,3)] and number of available cleavage embryos [3.0(2.0,4.5) vs. 1.0(0,2.0)] between the two groups (all $P<0.001$). 2) Multivariate logistic regression analysis suggested that age ($OR=0.878$, 95% $CI=0.846-0.911$, $P<0.001$) was the vital factor of cumulative delivery rate. The cumulative pregnancy rate and the cumulative delivery rate were significantly decreased with age increasing (all $P<0.001$). And the cancelation rate of group with age more than 40 years was much higher ($P<0.001$). **Conclusion** Age was the independent influencing factor of cumulative delivery rate. The cumulative delivery rate decreased significantly with age increasing.

【 Key words 】 Anti-Müllerian hormone; Cumulative delivery rate; Fertilization *in vitro*; Embryo transfer

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不同年龄患者全胚冷冻后首次冻融 胚胎移植的临床策略

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【摘要】 目的 探讨冷冻胚胎周期不同年龄段患者如何制定移植策略。方法 回顾性队列研究分析浙江省宁波市妇女儿童医院生殖中心取卵后全胚冷冻并于2018年1月至2020年4月期间首次行冻融胚胎移植患者的临床资料,根据患者的年龄分为三组,即 ≤ 30 周岁组(1150个周期)、30~35周岁组(932个周期)及 > 35 周岁组(405个周期);在每个年龄组内,再根据移植胚胎级别及移植数目分为第3日单卵裂期胚胎移植(single cleavage stage embryo transplant, SET3)亚组、第5日单囊胚移植(single 5th day blastocyst transplant, SET5)亚组、第6日单囊胚移植(single 6th day blastocyst transplant, SET6)亚组、第3日双卵裂期胚胎移植(double cleavage stage embryo transplant, DET3)亚组、第5日双囊胚移植(double 5th day blastocyst transplant, DET5)亚组、第6日双囊胚移植(double 6th day blastocyst transplant, DET6)亚组。所有患者均随访至2020年6月30日,比较同一年龄组内各亚组的临床结局。**结果** ① ≤ 30 周岁组: SET5亚组临床妊娠率、持续妊娠率及活产率分别为66.17%(221/334)、60.48%(202/334)及35.93%(120/334),分别高于SET3亚组[41.18%(28/68)、36.76%(25/68)、25.00%(17/68)], $P < 0.001$ 、 $P = 0.001$ 、 $P = 0.045$]及SET6亚组[54.42%(80/147)、43.54%(64/147)、27.21%(40/147)], $P < 0.001$ 、 $P = 0.001$ 、 $P < 0.001$]; DET5亚组多胎率[47.80%(76/159)]高于DET6亚组[29.49%(23/78)] ($P = 0.007$)。②30~35周岁组: SET5亚组临床妊娠率、持续妊娠率及活产率分别为63.59%(138/217)、55.30%(120/217)及29.95%(65/217),分别高于SET3亚组[30.65%(19/62)、27.42%(17/62)、14.52%(9/62)], $P < 0.001$ 、

$P<0.001$ 、 $P=0.015$]; DET5 亚组多胎率[56.86%(58/102)]高于 DET3 亚组[32.54%(41/126)]及 DET6 亚组[28.57%(16/56)], 差异均有统计学意义($P<0.001$ 及 $P=0.001$)。③35 周岁以上组: SET5 亚组临床妊娠率、持续妊娠率及活产率[53.45%(31/58)、39.66%(23/58)、20.69%(12/58)]与 SET6 亚组[43.75%(21/48)、35.42%(17/48)、16.76%(8/48)]比较, 差异均无统计学意义($P=0.320$ 、 $P=0.655$ 、 $P=0.583$), 高于 SET3 亚组[16.98%(9/53)、15.09%(8/53)、7.55%(4/53)], $P<0.010$ 、 $P=0.004$ 、 $P=0.049$]; DET5 亚组临床妊娠率及持续妊娠率[66.67%(26/39)、53.85%(21/39)]均高于 DET3 亚组[33.89%(61/180)、27.22%(49/180)], 差异均有统计学意义($P<0.001$ 、 $P=0.001$); DET5 亚组临床妊娠率高于 DET6 亚组[51.85%(14/27)], 差异有统计学意义($P=0.001$)。结论 对各年龄组患者, 应尽量选择单胚胎移植, 避免移植 2 个第 5 日囊胚; 移植胚胎首选第 5 日单囊胚。

【关键词】 年龄; 冷冻; 胚胎移植; 妊娠率; 多胎

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Clinical strategy of the first frozen-thawed embryo transfer after cryopreservation in patients of different ages

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【Abstract】 **Objective** To explore how to make transplantation strategy for patients of different ages in frozen-thawed embryo (FET) cycle. **Methods** A retrospective cohort analysis of the first FET cycles during the period from January 2018 to April 2020 in Reproductive Center of Ningbo Women & Children Hospital was performed. Based on the age of the patients, they were divided into three groups: ≤ 30 years old group (1150 cycles), 30–35 years old group (932 cycles) and >35 years old group (405 cycles). In each age group, according to the grade and number of transferred embryos, they were divided into the single cleavage stage embryo transplant (SET3) subgroup, the single 5th day blastocyst transplant (SET5) subgroup, the single 6th day blastocyst transplant (SET6) subgroup, the double cleavage stage embryos transplant (DET3) subgroup, the double 5th day blastocyst transplant (DET5) subgroup and the double 6th day blastocyst transplant (DET6) subgroup. All patients were followed up until June 30, 2020. The clinical outcomes of each subgroups within the same age group were compared. **Results** 1) In ≤ 30 years old group: the clinical pregnancy rate, the persistent pregnancy rate and the live birth rate in SET5 subgroup were 66.17% (221/334), 60.48% (202/334), 35.93% (120/334), respectively, which were higher than those in SET3 subgroup [41.18% (28/68), 36.76% (25/68), 25.00% (17/68); $P<0.001$, $P=0.001$, $P=0.045$] and that in SET6 subgroup [54.42% (80/147), 43.54% (64/147), 27.21% (40/147); $P<0.001$, $P=0.001$, $P<0.001$]. The multiple rate in DET5 subgroup was 47.80% (76/159), which was higher than that in DET6 subgroup [29.49% (23/78), $P=0.007$]. 2) In 30–35 years old group: the clinical pregnancy rate, the persistent

pregnancy rate and the live birth rate in SET5 subgroup were 63.59% (138/217), 55.30% (120/217) and 29.95% (65/217), which were higher than those in SET3 subgroup [30.65% (19/62), 27.42% (17/62), 14.52% (9/62); $P<0.001$, $P<0.001$, $P=0.015$]. The multiple rate in DET5 subgroup was 56.86% (58/102), which was higher than that in DET3 subgroup [32.54% (41/126)] and DET6 subgroup [28.57% (16/56)], and the differences were statistically significant ($P<0.001$, $P=0.001$). 3) In >35 years old group: the clinical pregnancy rate, the sustained pregnancy rate and the live birth rate in DET5 subgroup were 53.45% (31/58), 39.66% (23/58), 20.69% (12/58), compared with those in SET6 subgroup [43.75% (21/48), 35.42% (17/48), 16.76% (8/48)], the differences were not statistically significant ($P=0.320$, $P=0.655$, $P=0.583$), while compared with SET3 subgroup [16.98% (9/53), 15.09% (8/53), 7.55% (4/53)], the differences were statistically significant ($P<0.010$, $P=0.004$, $P=0.049$). The clinical pregnancy rate and the sustained pregnancy rate in DET5 subgroup were 66.67% (26/39), 53.85% (21/39), which were higher than those in DET3 subgroup [33.89% (61/180), 27.22% (49/180)], and the differences were statistically significant ($P<0.001$, $P=0.001$). The clinical pregnancy rate in DET5 subgroup was higher than that in DET6 subgroup [51.85% (14/27)], and the difference was statistically significant ($P=0.001$). **Conclusion** For patients of all ages, single embryo transfer should be selected, and avoid the transfer of two 5th day blastocysts as far as possible. The 5th day single blastocyst is preferred for embryo transfer.

【Key words】 Age; Freezing; Embryo transfer; Pregnancy rate; Multiple

Fund program: Medical and Health Brand Discipline in Ningbo (PPXK2018-06); Zhejiang Medical and Health Science and Technology Project (2019RC268)

· 临床研究 ·

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移植囊胚数、质量评分及形成时间 对<38岁女性冻融周期临床结局的 影响

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【摘要】 目的 探讨移植囊胚数、质量及形成时间对<38岁女性冻融胚胎移植(frozen-thawed embryo transfer, FET)临床结局的影响。**方法** 回顾性队列研究分析2017年1月至2020年1月期间在中国人民解放军联勤保障部队第九〇一医院生殖中心行冻融囊胚移植且年龄<38岁女性1441个周期的临床资料。根据囊胚移植数、质量[内细胞团(inner cell mass, ICM)、外胚滋养层细胞(trophectoderm, TE)评分]分为单优质囊胚移植组(单优组)、双优质囊胚移植组(双优组);再根据囊胚移植数、质量及形成时间将非优质囊胚分为双BC级囊胚移植组(双BC组)、双CB级囊胚移植组(双CB组)、BC级+CB级双囊胚移植组(BC+CB组)、单BC级囊胚移植组(单BC组)、单CB级囊胚移植组(单CB组)、第5日(day 5, D5)单BC级囊胚移植组(D5单BC组)、D5单CB级囊胚移植组(D5单CB组)及第6日(day 6, D6)单BC级囊胚移植组(D6单BC组),比较各组的临床妊娠率、种植率、早期流产率、多胎妊娠率和异位妊娠率。**结果** 单优组的临床妊娠率、早期流产率、异位妊娠率与双优组间差异均无统计学意义(P 均>0.05),多胎妊娠率[2.96%(14/473)]则显著低于双优组[55.65%(69/124)]、双BC组[42.55%(20/47)]、双CB组[63.49%(473/745)比35.22%(31/83)]、BC+CB组[45.57%(36/79)](P <0.001);单优组的临床妊娠率和种植率显著高于单CB组[63.49%(473/745)比45.59%(30/68), 63.49%(473/745)比45.59%(30/68), P 均=0.002],与单BC组间差异无统计学意义(P >0.05),各单囊胚移植组间多胎妊娠率、早期流产率、异位妊娠率差异均无统计学意义(P 均>0.05);D5单BC组的临床妊娠率、种植率均显著高于D6单BC组[65.79%(50/76)比39.47%(15/38), 65.79%(50/76)比39.47%(15/38), P 均<0.001];D5单CB组的临床妊娠率、种植率均高于D6单BC组,但差异无统计学意义(P >0.05)。**结论** 冻融囊胚移植周期,年龄<38岁女性应行单优质囊胚移植;无优质囊胚时,应优先选择D5 ICM评分更高的单囊胚移植,其次选择D5 TE评分更高的单囊胚移植。

【关键词】 囊胚; 评分; 冻融胚胎移植; 临床结局

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Effects of transferred blastocyst quantity, quality score and formation time on clinical out-comes of frozen-thawed cycles in the women aged less than 38 years old

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【Abstract】 Objective To investigate the effects of transferred blastocyst quantity, quality and formation time on the clinical outcomes of frozen-thawed embryo transfer (FET) cycles in the women aged less than 38 years old. **Methods** The data of 1441 frozen-thawed blastocyst transfer cycles in the women aged less than 38 years between January 2017 and January 2021 in Reproductive Medical Center of the 901th Hospital of PLA were analyzed in this retrospective cohort study. According to the number and grade [scored by the inner cell mass (ICM), trophoctoderm (TE)] of transferred blastocyst, the patients were divided into single good-quality blastocyst group and double good-quality blastocyst group. Then, based on the quantity, quality and formation time of the transferred blastocysts, the non-good-quality ones were subdivided into double BC group, double CB group, BC+CB group, single BC group, single CB group, single day 5 (D5) BC group, single D5 CB group and single day 6 (D6) BC group. The clinical pregnancy rate, the implantation rate, the early abortion rate, the multiple pregnancy rate and the ectopic pregnancy rate were compared among the groups. **Results** There were no statistically significant differences in the clinical pregnancy rate, the early abortion rate and the ectopic pregnancy rate between single good-quality group and double good-quality group ($P>0.05$), while the multiple pregnancy rate [2.96% (14/473)] in single good-quality blastocyst group was significantly lower than that in double good-quality blastocyst group [55.65% (69/124)], double BC group [42.55% (20/47)], double CB group [35.22% (31/83)] and [55.65% (69/124)], double BC group [42.55% (20/47)], double CB group [35.22% (31/83)] and BC+CB group [45.57% (36/79)] ($P<0.001$). The clinical pregnancy rate and the implantation rate in single good-quality blastocyst group were significantly higher than those in the single CB group (63.49% vs. 45.59%, 63.49% vs. 45.59%, all $P=0.002$), but comparable to those in single BC group [63.49% (473/745) vs. 45.59% (65/114), 63.49% (473/745) vs. 45.59% (65/114), all $P=0.002$]. There were no statistically significant differences in multiple pregnancy rate, miscarriage rate and ectopic pregnancy rate among single good-quality blastocyst group, single BC group and single CB group ($P>0.05$). The clinical pregnancy rate and the implantation rate in D5 single BC group were higher than those in D6 single BC group [65.79% (50/76) vs. 39.47% (15/38), 65.79% (50/76) vs. 39.47% (15/38), all $P<0.001$]. Moreover, the clinical pregnancy rate and the implantation rate in D5 single CB group were higher than those in D6 single BC group, but there was no significantly different. **Conclusion** Single good-quality blastocyst transfer should be performed for the women aged less than 38 years in FET cycles. When there is no good-quality blastocyst, it is preferable to choose single D5 non-good-quality blastocyst with higher ICM score for transfer, then choose the one with higher TE score.

【Key words】 Blastocyst; Score; Frozen-thawed embryo transfer; Clinical outcomes

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非排卵障碍不孕患者宫腔内夫精人工授精自然周期与促排卵周期妊娠结局分析

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【摘要】 目的 探讨分析非排卵障碍不孕患者接受自然周期与促排卵周期宫腔内夫精人工授精的妊娠结局。方法 回顾性队列研究分析 2014 年 1 月至 2019 年 10 月期间就诊于杭州市妇产科医院, 年龄 ≤ 35 岁, 因非排卵障碍不孕就诊的患者共 821 个周期, 按照是否促排卵分为自然周期组 (N 组), 共 225 个周期; 促排卵周期组 (O 组), 共 596 个周期; 按照宫腔内夫精人工授精不孕的原因 [不明原因不孕 (A), 男方精液异常 (B), 性功能障碍 (C), 单侧输卵管梗阻 (D)] 分为 4 个亚组, 分别为 NA 组 (67 例)、NB 组 (94 例)、NC 组 (39 例)、ND 组 (25 例) 和 OA 组 (233 例)、OB 组 (217 例)、OC 组 (51 例)、OD 组 (95 例)。比较 N 组患者和 O 组患者一般资料、临床妊娠率、流产率、异位妊娠率、多胎妊娠率等指标; 比较各亚组之间临床妊娠率、流产率、异位妊娠率、多胎妊娠率。结果 ①N 组和 O 组患者临床妊娠率、流产率、异位妊娠率之间比较, 差异均无统计学意义 (P 均 >0.05), 但是 O 组多胎妊娠率为 13.1% (13/99), 明显高于 N 组的 0% (0/30), 差异有统计学意义 ($P=0.038$)。②NA 组、NB 组、NC 组、ND 组和 OA 组、OB 组、OC 组、OD 组之间临床妊娠率、流产率、异位妊娠率、多胎妊娠率比较差异均无统计

学意义 (P 均 >0.05)。结论 对于非排卵障碍不孕患者进行宫腔内夫精人工授精助孕治疗时,促排卵周期并不能提高患者的临床妊娠率,反而会增加多胎妊娠率。

【关键词】 宫腔内人工授精; 妊娠结局; 促排卵周期; 自然周期

基金项目:浙江省医药卫生科技计划项目 (2020KY764)

Analysis of the clinical pregnancy outcomes of infertile patients with non-ovulation disorder receiving natural cycle or ovulation induction cycle with artificial intrauterine insemination with the husband's sperm

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【 Abstract 】 Objective To explore the pregnancy outcomes of non-ovulation disorder infertile patients with natural cycle or ovulation-promoting cycle of intrauterine insemination (IUI) with the husband's sperm. **Methods** A retrospective cohort study was carried out on a total of 821 cycles of non-ovulation disorder infertile patients who received IUI with ≤ 35 years old at the Hangzhou Women's Hospital from January 2014 to October 2019. According to whether the ovulation induction, they were divided into natural cycle group (group N, $n=225$) and ovulation induction cycle group (group O, $n=596$). Meanwhile, according to the etiology of IUI infertility [unexplained infertility (A), men's semen abnormalities (B), sexual dysfunction (C), unilateral tubal obstruction (D)], they were divided into four subgroups, namely NA group ($n=67$), NB group ($n=94$), NC group ($n=39$), ND group ($n=25$) and OA group ($n=233$), OB group ($n=217$), OC group ($n=51$), OD group ($n=95$). The general information, clinical pregnancy rate, abortion rate, ectopic pregnancy rate, multiple pregnancy rate, and other indicators of patients were compared between group N and group O. Clinical pregnancy rate, abortion rate, ectopic pregnancy rate, and multiple pregnancy rate were compared between each two subgroups. **Results** 1) The multiple pregnancy rate of ovulation induction cycle group was 13.1% (13/99), more than 0% (0/30) of natural cycle group, the differences was statistically significant ($P=0.038$). There were no significant differences between the two groups in clinical pregnancy rate, abortion rate, and ectopic pregnancy rate (all $P>0.05$). 2) There were no significant differences between each two subgroups in clinical pregnancy rate, abortion rate, ectopic pregnancy rate and multiple birth rate (all $P>0.05$). **Conclusion** For non-ovulatory infertile patients with IUI, the ovulation induction may not increase the clinical pregnancy rate of the patient, but may increase the multiple birth rate.

【Key words】 Artificial insemination with intrauterine; Pregnancy outcome; Ovulation induction cycle; Natural cycle

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子宫体积对子宫腺肌病合并不孕症患者新鲜胚胎移植临床结局的影响

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【摘要】 目的 探讨胚胎移植前子宫体积对子宫腺肌病患者新鲜胚胎移植临床结局的影响。方法 回顾性队列研究 2009 年 1 月至 2018 年 12 月期间年龄 ≤ 40 岁因子宫腺肌病合并不孕症于北京大学第三医院妇产科生殖医学中心首次行超长方案体外受精/卵胞质内单精子注射-胚胎移植(*in vitro fertilization/intracytoplasmic sperm injection-embryo transfer*, IVF/ICSI-ET)助孕患者的临床资料。根据移植前子宫体积将研究对象分为 A 组($56\sim 90\text{ cm}^3$, 子宫体积如妊娠 6 周之内)、B 组($90\sim 130\text{ cm}^3$, 子宫体积如妊娠 6~8 周)和 C 组($\geq 130\text{ cm}^3$, 子宫体积如妊娠 8 周以上), 比较不同子宫体积对临床结局的影响。logistic 回归分析移植前子宫体积与临床结局的相关性。结果 共纳入 232 名患者, 其中 A 组 153 例、B 组 52 例、C 组 27 例。三组患者的年龄、体质指数(body mass index, BMI)、基础卵泡刺激素(follicle-stimulating hormone, FSH)水平、窦卵泡数、不孕类型、子宫内膜厚度、获卵数、受精方式、可移植胚胎数与移植胚胎数差异均无统计学意义(P 均 >0.05)。三组患者的临床妊娠率差异无统计学意义($P>0.05$)。A 组流产率为 24.59% (15/61), B 组流产率为 64.71% (11/17), C 组流产率为 55.56% (5/9), 组间比较差异有统计学意义($P=0.004$)。B 组的活产率 [11.54% (6/52)] 低于 A 组 [30.07% (46/153)], 差异有统计学意义($P=0.009$)。logistic 回归分析结果显示, 移植前子宫体积与临床妊娠率无显著相关性 ($OR=0.762$, 95% $CI=0.481\sim 1.208$, $P=0.248$), 与流产率呈显著正相关 ($OR=2.822$, 95% $CI=1.165\sim 6.835$, $P=0.022$), 与活产率呈显著负相关 ($OR=0.458$, 95% $CI=0.238\sim 0.881$, $P=0.019$)。结论 子宫腺肌病合并

不孕症患者胚胎移植前子宫体积增大 (尤其是 $>90\text{ cm}^3$) 时流产率增加, 活产率降低。提示对于子宫腺肌病患者控制子宫体积仍是提高 IVF-ET 临床结局的关键。

【关键词】 受精, 体外; 子宫腺肌病; 流产; 活产; 子宫体积

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Effect of uterine volume on fresh embryo transfer outcomes in infertile patients with adenomyosis

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【Abstract】 Objective To investigate the impact of uterine volume prior to fresh embryo transfer on reproductive outcomes in infertile patients with adenomyosis. **Methods** A retrospective cohort study was conducted for the clinical data of patients diagnosed with adenomyosis and aged ≤ 40 years undergoing *in vitro* fertilization/intracytoplasmic sperm injection-embryo transfer (IVF/ICSI-ET) with ultra-long downregulation stimulation protocol in Center for Reproductive Medicine, Department of Obstetrics and Gynecology of Peking University Third Hospital between January 2009 and December 2018. Logistic regression model was used to analyze the correlation between uterine volume and clinical outcomes. Study subjects were divided into three groups based on uterine volume before embryo transfer: group A $56\text{--}90\text{ cm}^3$ (equivalent to uterine size within 6 weeks of pregnancy); group B $90\text{--}130\text{ cm}^3$ (equivalent to 6–8 weeks gestation); group C $\geq 130\text{ cm}^3$ (equivalent to uterine size greater than 8 weeks gestation), the effect of uterine volume on clinical outcomes was compared. **Results** Totally 232 patients were included, 153 patients in group A, 52 patients in group B, 27 patients in group C. The data showed no statistical difference among the three groups in basic characteristics ($P>0.05$). There was no significant difference in clinical pregnancy rate among three groups ($P>0.05$). The incidence of miscarriage among three groups were significantly different [group A, 24.59% (15/61); group B, 64.71% (11/17); group C, 55.56% (5/9), $P=0.018$]. Compared with group A [30.07% (46/153)], the live birth rate of group B [11.54% (6/52)] was significantly reduced ($P=0.009$). Logistic regression analysis showed that uterine volume before ET was not related to clinical pregnancy rate ($OR=0.762$, 95% $CI=0.481\text{--}1.208$, $P=0.248$), and was positively related to miscarriage rate ($OR=2.822$, 95% $CI=1.165\text{--}6.835$, $P=0.022$) while negatively correlated with live birth rate ($OR=0.458$, 95% $CI=0.238\text{--}0.881$, $P=0.019$). **Conclusion** An increased level of uterine volume prior to embryo transfer (especially larger than 90 cm^3) increases miscarriage rate and reduces the live birth rate in infertile patients with adenomyosis. Therefore, controlling uterine volume is still a key to improve the clinical outcome of IVF-ET in adenomyosis patients.

【Key words】 Fertilization *in vitro*; Adenomyosis; Abortion; Live birth;
Uterine volume

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·临床报道·

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子宫内膜癌保守治疗后的不孕患者 带左炔诺孕酮宫内节育系统行体外 受精助孕的临床分析

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【摘要】 目的 探讨高分化子宫内膜样癌 (endometrial carcinoma, EC) 及子宫内膜不典型增生 (atypical endometrial hyperplasia, AEH) 合并不孕患者在病变逆转后置入左炔诺孕酮宫内节育系统 (曼月乐) 再行体外受精 (*in vitro* fertilization, IVF) 助孕的临床策略可行性。方法 回顾性分析了 2018 年 3 月至 2019 年 12 月期间就诊于中国医学科学院北京协和医院妇科内分泌与生殖中心的 20 例 EC 及 AEH 合并不孕症患者的临床资料。所有患者保守治疗成功后带曼月乐行 IVF 促排卵周期。取卵后胚胎培养至囊胚并冷冻, 累积冷冻 ≥ 4 枚囊胚后, 所有患者取环并评估内膜组织学, 观察冷冻周期移植囊胚的临床结局。结果 患者中位年龄为 33 岁, 内膜诊刮病理评估首次达完全缓解时间为 4.3 个月。共进行取卵周期 34 个, 中位获卵数为 8 枚; 共尝试解冻周期 21 个, 实际可移植胚胎的周期为 14 个, 5 例临床妊娠, 3 例继续妊娠。结论 对于内膜病变逆转后的 EC 及 AEH 合并不

孕症患者,带曼月乐进行 IVF 时待获得足够囊胚后再取环移植可能是一种可行的助孕策略。

【关键词】 不孕症； 子宫内膜样腺癌； 子宫内膜不典型增生； 受精，体外； 胚胎移植； 左炔诺孕酮宫内节育系统

Clinical analysis of infertility patients undergoing *in vitro* fertilization with a levonorgestrel intrauterine system *in situ* after conservative treatment of early well-differentiated endometrial adenocarcinoma and atypical endometrial hyperplasia

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【Abstract】 Objective To investigate the feasibility of a novel *in vitro* fertilization (IVF) strategy with levonorgestrel intrauterine system (Mirena) *in situ* in infertility patients after successful conservative treatment of early well-differentiated endometrial adenocarcinoma (EC) and atypical endometrial hyperplasia (AEH). **Methods** The clinical characteristics of infertility patients after a complete regression of previous EC and AEH who underwent IVF with a Mirena *in situ* from March 2018 to December 2019 in Center for Gynecological Endocrinology & Reproductive Medicine, Peking Union Medical College Hospital were retrospectively analyzed. These patients underwent one or more cycles to harvest at least 4 blastocysts cryopreserved, before removing the Mirena and re-evaluating the endometrium. Then the outcomes of frozen-thawed embryo transfer (FET) were commenced. **Results** A total of 20 patients were included with a median age of 33 years. The complete regression of endometrial lesion was achieved at 4.3 months. Thirty-four IVF cycles were conducted in total, leading to a median oocytes retrieved of 8. We had attempted 21 embryo transfer but only 14 cycles were effective, and 5 patients got clinical pregnancy and 2 patients had ongoing pregnancy. **Conclusion** It is a supposedly practical way that IVF with the Mirena until pooling enough blastocysts before removing the device and initiating embryo transfer for assisting reproduction and endometrial protection in patients after fertility-sparing treatment of EC or AEH.

【Key words】 Infertility; Endometrial adenocarcinoma; Endometrial hyperplasia with atypia; Fertilization *in vitro*; Embryo transfer; Levonorgestrel intrauterine system

· 个案报道 ·

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体外受精-胚胎移植术后卵巢妊娠合并输卵管妊娠 1 例报道

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【摘要】 目的 报道 1 例体外受精-胚胎移植 (*in vitro* fertilization and embryo transfer, IVF-ET) 术后发生的输卵管妊娠合并卵巢妊娠，总结 IVF-ET 术后发生复合妊娠的临床特点，为预防 IVF-ET 术后复合妊娠的发生以及治疗提出建议。方法 对本院 1 例 IVF-ET 术后发生的输卵管妊娠合并卵巢妊娠病例进行详细阐述及分析。查阅文献并总结学习。结果 输卵管妊娠合并卵巢妊娠系极为罕见的一种复合妊娠，但 IVF-ET 术后其发生的可能性较高，移植胚胎的类型、位置及数量均为其发生的危险因素，需要临床医生警惕。结论 IVF-ET 术后复合妊娠一旦发现应及时处理。

【关键词】 生殖技术，辅助； 输卵管妊娠； 卵巢妊娠

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A case report of tubal pregnancy combined with ovarian pregnancy after assisted reproductive technology

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【Abstract】 **Objective** To report a case of tubal pregnancy combined with ovarian pregnancy after assisted reproductive technology and puts forward suggestions for prevention and treatments for heterotopic pregnancy after *in vitro* fertilization and embryo transfer (IVF-ET). **Methods** A case of tubal combined with ovarian pregnancy after IVF-ET was reported in detail, meanwhile a series of literatures were reviewed and summarized. **Results** Tubal pregnancy with

ovarian pregnancy is an extremely rare heterotopic pregnancy while the rate of heterotopic pregnancy is increasing after IVF-ET. Different types of embryo and locations of embryos transferred, as well as the number of transferred embryos, can be related to the occurrence of heterotopic pregnancy. **Conclusion** Heterotopic pregnancy after IVF-ET should be treated timely.

【Key words】 Reproductive technology, assisted; Tubal pregnancy; Ovarian pregnancy

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· 个案报道 ·

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卵巢过度刺激综合征合并卵巢出血的诊治体会 ——附 2 例病案报道与文献复习

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【摘要】 目的 探讨超声引导下穿刺取卵术 (transvaginal oocyte retrieval, TVOR) 后卵巢过度刺激综合征 (ovarian hyperstimulation syndrome, OHSS) 合并卵巢出血的鉴别诊断、高危因素及治疗体会。方法 回顾性分析 2018 年 9 月至 2019 年 9 月期间郑州大学第一附属医院生殖与遗传专科医院收治的取卵术后 OHSS 合并卵巢出血 2 例患者资料并进行文献复习。结果 取卵术后 OHSS 合并卵巢出血 2 例均为多囊卵巢综合征 (polycystic ovary syndrome, PCOS) 患者, 表现为红细胞计数及血红蛋白含量下降、D-二聚体及纤维蛋白 (原) 降解物 (fibrinogen degradation product, FDP) 升高、心率加快、卵巢增大、超声提示盆腔无回声区及混合性包块。1 例保守治疗, 1 例手术治疗。结论 OHSS 重在预防, 取卵术后动态评估血常规可尽早发现卵巢出血, 同时机体产生保护性反应导致

D-二聚体及 FDP 在 OHSS 病理生理基础上进一步升高,需密切监测预防血栓形成。

OHSS 合并卵巢出血手术难度大且术后存在卵巢穿刺点活动性出血可能。

【关键词】 卵巢过度刺激综合征; 卵巢出血; 超声引导下穿刺取卵术;
D-二聚体; 纤维蛋白(原)降解物

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Diagnosis and treatment of ovarian hyperstimulation syndrome complicated with ovarian hemorrhage: two cases report and literature review

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【Abstract】 **Objective** To investigate the differential diagnosis, risk factors and treatment strategies of ovarian hyperstimulation syndrome (OHSS) complicated with ovarian hemorrhage after transvaginal oocyte retrieval (TVOR). **Methods** A retrospective clinical study and a literature review were performed to analyze 2 cases of OHSS complicated with ovarian hemorrhage after TVOR from September 2018 to September 2019 in the Reproductive Medical Center, the First Affiliated Hospital of Zhengzhou University. **Results** Two cases of OHSS complicated with ovarian hemorrhage after TVOR were both patients with polycystic ovary syndrome (PCOS), showing the decline of red blood cell and hemoglobin, the increase of D-dimer, fibrinogen degradation product (FDP), heart rate and ovarian size, and pelvic anechoic area and mixed mass in ultrasonogram. One was under conservative treatment, and the other underwent a surgery. **Conclusion** Continuous assessment of blood routine can detect hemorrhage early after TVOR. In the meanwhile, the body produces a protective response which contributes to the further rise of D-dimer and FDP on the basis of the pathophysiology characteristics of OHSS. As a result, doctors need to monitor the blood routine closely and prevent thrombosis. The surgery of OHSS combined with ovarian hemorrhage is difficult and there may be active bleeding at the ovarian puncture point after surgery.

【Key words】 Ovarian hyperstimulation syndrome; Ovarian hemorrhage; Transvaginal oocyte retrieval; D-dimer; Fibrinogen degradation product

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· 个案报道 ·

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PATL2 基因的复合杂合突变导致以卵母细胞成熟停滞为特征的不孕

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【摘要】 目的 探索卵母细胞成熟停滞的遗传学病因。方法 收集 2018 年在海军军医大学附属长海医院生殖医学中心一对患有原发性不孕症的姐妹的临床资料。用二代测序的方法对患者做全基因组测序, 检测到 *PATL2* 基因的两个突变位点。然后对该家庭中所有成员和健康人的两个突变位点附近区域扩增并进行一代测序验证。进一步通过生物信息学分析, 探索疾病的发病机制。结果 这对姐妹中鉴定了 *PATL2* 基因的复合杂合突变: 一个错义突变 (p. V260M) 和一个剪接突变 (p. R75Vfs*21), 这两个突变已经被报道过。这两个突变都通过引起 mRNA 异常剪接导致基因功能异常。结论 本案例验证了 *PATL2* 基因突变与人卵母细胞成熟停滞之间的相关性, 并为卵母细胞和胚胎的质量评价提供分子生物标志物。

【关键词】 卵母细胞成熟停滞; *PATL2* 基因; 突变; 不孕

基金项目: 国家重点研发计划 (2018YFC1005002)

Complex heterozygous mutations in *PATL2* result in female infertility characterized by oocyte maturation arrest

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【 Abstract 】 Objective To explore the genetic causes of oocyte maturation arrest. **Methods** A pair of sisters with primary infertility was collected in the Reproductive Medicine Center of Changhai Hospital, Naval Medical University in 2018. Two *PATL2* mutations were found in the patients by second-generation whole genome sequencing. Then, for all members of the family and a healthy control person, the regions near the two mutation sites were amplified and sequenced by Sanger sequencing to verify the two mutations. Furthermore, the pathogenesis of the disease was explored through bioinformatics analysis. **Results** Compound heterozygous mutations of *PATL2* were identified in the two sisters: a missense mutation (p.V260M) and a splicing mutation (p.R75Vfs*21). Both mutations have been reported, and they both cause abnormal splicing of *PATL2* mRNA, leading to abnormal gene function. **Conclusion** Our

study confirmed the correlation between *PATL2* mutations and human oocyte maturation arrest, and it provided molecular biomarkers for oocyte and embryo quality assessment.

【Key words】 Oocyte maturation arrest; *PATL2* gene; Mutation; Infertility

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· 专家视角 ·

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雌、孕激素暴露时间及其血清浓度对人工周期冻融胚胎移植结局的影响

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【摘要】 近年来, 随着辅助生殖技术的不断发展, 冻融胚胎移植 (frozen-thawed embryo transfer, FET) 周期数不断增多, 而激素替代疗法 (hormone replacement therapy, HRT) 是 FET 周期准备子宫内膜的主要方法之一。HRT-FET 周期中雌、孕激素的暴露时间及血清雌、孕激素水平是否影响 FET 的成功率? 是否可以以此为切入点, 改善 FET 的治疗结局? 本文对此进行了综述。在 HRT-FET 周期, 给予孕激素前过短时间的雌激素暴露可能增加早期流产率, 血清雌激素水平与治疗结局无相关性。胚胎移植前孕激素的暴露时间影响治疗结局, 胚胎移植日血清孕激素水平是持续妊娠和活产的独立预后因素。

【关键词】 冻融胚胎移植; 激素替代疗法; 雌激素; 孕激素; 人工周期

Effects of estrogen and progesterone exposure time and serum concentrations on the outcomes of frozen-thawed embryo transfer in artificial cycles

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【 Abstract 】 With the continuous development of assisted reproductive technology recently, frozen-thawed embryo transfer (FET) cycles are increasing, and hormone replacement therapy (HRT) is one of the main methods for preparing endometrium in FET cycles. Do the exposure time of estrogen and progesterone and the levels of serum estrogen and progesterone affect the success rate of FET? Can we use this as an entry point to improve the treatment outcome of FET? This article reviews papers in this field. In the HRT-FET cycle, short-term estrogen exposure before progestin administration might increase early miscarriage rate, and serum estrogen levels are not related to treatment outcome. The progesterone exposure time before embryo transfer affects the outcome of FET. The serum progesterone level on the day of embryo transfer is an independent prognostic factor for ongoing pregnancy and live birth.

【 Key words 】 Frozen-thawed embryo transfer; Hormone replacement therapy; Estrogen; Progesterone; Artificial cycle

· 综 述 ·

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辅助生殖技术治疗对妊娠结局及女性远期健康影响的研究进展

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【摘要】 辅助生殖技术 (assisted reproductive technology, ART) 为不孕症女性提供了生育的机会, 但是治疗过程中涉及的非生理性干预可能会通过影响

妊娠大环境增加母体严重不良妊娠结局的发生风险。另外，促排卵药物的使用，如枸橼酸氯米芬（克罗米芬）、促性腺激素等会使机体性激素水平升高，反复周期性使用促排卵药物是否增加女性远期罹患乳腺癌、子宫内膜癌和卵巢癌等妇科肿瘤的风险，以及内分泌代谢系统和心血管系统的远期并发症等风险是否增加，目前也尚无定论。由于 ART 治疗患者的年龄、体质量指数、基础慢性疾病和不孕原因等都可能是混杂因素，需要进一步随访并利用大数据，逐渐明确 ART 对女性妊娠结局及远期健康的影响，为临床医生制定临床决策和个体化的治疗方案提供重要参考依据。

【关键词】 生殖技术， 辅助； 妊娠并发症； 内分泌系统疾病； 乳腺肿瘤； 生殖器肿瘤， 女性

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Research progress on assisted reproductive technology effects on pregnancy outcomes and women's long-term health

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【Abstract】 Assisted reproductive technology (ART) offers infertile women the chance to have children, but the unphysiological interventions involved in the treatment may increase the risk of a serious adverse pregnancy outcome by affecting the pregnancy environment. In addition, the use of ovulation drugs, such as clomiphene citrate, gonadotrophin, make the body sex hormone levels rise. Whether periodic use of stimulating ovulation drugs repeatedly increases the risk of breast cancer and gynecological tumors, such as endometrial cancer and ovarian cancer, as well as endocrine metabolism system disorders and cardiovascular system diseases has not been determined. Furthermore, the patient's age, body mass index, underlying chronic disease and infertility factors are all likely to be confounding factors. It needs more further follow-up cohort study and uses big data to clarify ART influence on female pregnancy outcomes and the long-term health gradually. It will provide important reference data for reproductive doctors to make reasonable treatment plan according to the specific condition of patients with the purpose of protecting women's long-term health.

【Key words】 Reproductive techniques, assisted; Pregnancy complications; Endocrine system diseases; Breast neoplasms; Genital neoplasms, female

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· 综 述 ·

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胚胎植入前的无创评估技术新进展

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【摘要】 作为一种延续后代的重要辅助手段，人类辅助生殖技术 (assisted reproductive technology, ART) 在临床的应用越来越广泛。胚胎植入前的形态学评估和遗传学筛查是现代 ART 的一大重要组成部分，同时也是提高胚胎种植率和临床妊娠率的重要手段。现有的胚胎植入前遗传学筛查方法，由于其对胚胎活检的需求，安全性一直受到质疑。如何实现胚胎植入前筛查的无创性成为现阶段的研究热点。本文主要讨论了近年来一些具有临床应用价值的方法或技术，希望为无创筛查的临床应用提供参考。

【关键词】 受精，体外； 胚胎移植； 实时观测系统； 无创植入前遗传学检测； 蛋白质组学； 转录组学； 代谢组学

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New advances in noninvasive preimplantation screening

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【Abstract】 Assisted reproductive technology (ART), as an important means of procreation, has been increasingly applied to clinical practice. Morphological evaluation and genetic screening before embryo implantation is an important part of modern ART and an essential means to improve embryo implantation rate and clinical pregnancy rate. The safety of existing preimplantation genetic screening methods has been questioned due to their needs for embryo biopsies. How to achieve non-invasive preimplantation screening has become a research hotspot at the present stage. This paper mainly discusses some methods or technologies with clinical value in recent years, hoping to provide references for the clinical application of non-invasive screening.

【Key words】 Fertilization *in vitro*; Embryo transfer; Time lapse monitoring; Non-invasive preimplantation genetic test; Proteomics; Transcriptomics; Metabonomics

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· 综 述 ·

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粒细胞集落刺激因子在妊娠中的调节机制及其在不明原因复发性流产治疗中的研究进展

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【摘要】 不明原因复发性流产 (unexplained recurrent spontaneous abortion, URSA) 是妇科常见病及疑难病，其发病率呈逐年上升趋势。母-胎界面免疫耐受失衡是其重要原因之一。近年来的研究表明，粒细胞集落刺激因子 (granulocyte colony-stimulating factor, G-CSF) 是一种参与调控母-胎界面免疫功能的细胞因子，在胚胎着床、胎盘及胎儿发育过程中发挥重要作用。本文就 G-CSF 在正常妊娠过程中的作用机制及其在 URSA 治疗中应用的研究进展做一综述，以期为 URSA 病理机制和临床干预技术的进一步研究提供参考。

【关键词】 粒细胞集落刺激因子；不明原因复发性流产；免疫耐受

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Regulation mechanism of granulocyte colony-stimulating factor in pregnancy and its research progress in the treatment of unexplained recurrent miscarriage

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【 Abstract 】 Unexplained recurrent spontaneous abortion (URSA) is a common and difficult disease in gynecology, and its incidence is increasing year by year. Imbalance of the maternal-fetal interface immune tolerance is one of the important reasons. Recent studies have shown that granulocyte colony-stimulating factor (G-CSF) is a cytokine involved in regulating the immune function of maternal-fetal interface and plays an important role in embryo implantation, placenta and fetal development. This article reviews the research progress of the mechanism of G-CSF in normal pregnancy and its application in URSA treatment, in order to provide reference for further research on the pathological mechanism and clinical intervention technology of URSA.

【 Key words 】 Granulocyte colony-stimulating factor; Unexplained recurrent miscarriage; Immune tolerance

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左炔诺孕酮宫内缓释系统对育龄妇女生活质量的影响

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【摘要】 左炔诺孕酮宫内缓释系统 (levonorgestrel releasing intrauterine system, LNG-IUS) 是国内常见的宫内节育器 (intrauterine device, IUD) 之一，具有单纯孕激素避孕药具和 IUD 的特性，具有长效、可逆、安全的避孕效果，并在临床上被用于辅助治疗多种妇科疾病。“性”和“避孕”是人类繁衍的必修课，随着健康水平的提升，女性在选择避孕措施的同时更加关注性生活质量及生殖健康。本文结合国内外研究，重点探讨 LNG-IUS 作为含激素的 IUD 对使用者性生活质量的影响，为育龄妇女选择避孕措施提供参考依据。

【关键词】 左炔诺孕酮宫内缓释系统；性；生活质量

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Effects of levonorgestrel releasing intrauterine system on sexual life quality in women of reproductive age

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【Abstract】 Levonorgestrel releasing intrauterine system (LNG-IUS), an intrauterine device (IUD) containing slowly released progestogen, is the common IUD in China. LNG-IUS is not only a long-term, reversible and safe contraceptive method, but also used in the adjuvant treatment of some gynecological diseases. Nowadays, women are more concerned about the quality of sex life and reproductive health when choosing their contraceptive methods. This review will focus on the present researches and summarize the effects of LNG-IUS on users' sexual life quality, to provide references for the choice of contraceptive methods.

【Key words】 Levonorgestrel releasing intrauterine system; Sexuality; Quality of life

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