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宫内节育器临床研究设计与统计分析 专家共识

中华医学会儿计划生育学分会

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【摘要】 我国现有宫内节育器 (IUD) 使用者超过 1 亿, 约占世界使用总数的三分之二, 但我国 IUD 临床研究总体质量不高, 不利于保护广大育龄妇女的生殖健康。为指导国内医务工作者合理选择和使用 IUD 临床研究设计和统计分析方法, 中华医学会儿计划生育学分会专家经充分讨论并结合我国实际制定本共识。共识指出, IUD 临床研究全过程都应从流行病学与统计学角度考虑问题, 包括但不限于以下内容: ①明确研究问题, 将其转换为可用数据回答的统计问题; ②根据研究问题和实施条件匹配合理的研究设计, 并考虑研究设计控制混杂和偏倚的能力; ③在考虑混杂因素的基础上制定数据采集的内容和工作计划, 按计划采集和整理数据; ④合理选择分析数据集, 并使用恰当的统计方法。当受试者特征分布不均衡时, 应采用分层、倾向性评分、多元统计等方法进行数据分析; ⑤分析结果的解释应回应原始研究问题, 研究结论外推要考虑研究对象的代表性。

【关键词】 宫内节育器; 临床研究设计; 统计分析; 共识

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· 规范与标准 ·

Chinese experts' consensus on study design and statistical analysis for intrauterine device clinical research

Chinese Society of Family Planning Chinese Medical Association

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【Abstract】 To date, the number of intrauterine device (IUD) users in China is more than 100 million, accounting for about two thirds of the world IUD users. Previous studies showed that the overall quality of IUD clinical researches in China was low, which potentially threatened women's reproductive health. After a full discussion, experts from Chinese Society of Family Planning China Medical Association initiated and developed this consensus, which aimed to instruct Chinese clinicians to correctly use study designs and statistical analysis methods to carry out IUD clinical studies. This consensus points out that all kinds of IUD clinical studies should follow principals of epidemiology and medical statistics, including but not limited 1) define study questions and transform them into statistical items that can be answered by figures; 2) select correct types of clinical study designs, which based on study questions, practical conditions and the ability of confounding control of the adopted study design; 3) develop case report forms and data collect plan, considering the known confounding; collect and clean up study data as planned; 4) select a proper dataset that minimizes potential risks of biases and confounding and employ correct statistical methods for data analysis. If the distribution of participants' characteristics is imbalanced, stratifying analysis, propensity score and/or multivariable regression analysis should be used to controll potential confounding; 5) finding interpretations should answer the original study questions. Extrapolation of results from IUD clinical studies should consider the representativeness of study participants.

【Key words】 Intrauterine device; Clinical study design; Statistical analysis; Consensus

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生长激素在薄型子宫内膜患者冻融胚胎移植周期内膜准备中应用的临床研究

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【摘要】目的 探讨薄型子宫内膜患者冻融胚胎移植 (FET) 周期使用激素替代联合生长激素 (growth hormone, GH) 准备内膜的有效性。**方法** 采用前瞻性队列研究, 选取 2017 年 1 月至 2019 年 6 月期间就诊于沈阳九州家圆医院生殖中心, 既往因人绒毛膜促性腺激素 (hCG) 注射日内膜厚度 <7 mm 取消新鲜周期移植拟 FET 的患者。经患者知情同意, 根据患者意愿分成 3 组: A 组激素替代同时宫腔灌注 GH ($n=76$); B 组激素替代同时给予皮下注射 GH ($n=72$); C 组单纯激素替代治疗 ($n=66$)。比较 3 组间患者基本情况及 FET 预后指标。**结果** 3 组间患者的年龄、不孕年限、体质量指数 (BMI)、基础卵泡刺激素 (FSH)、基础黄体生成素 (LH)、基础雌二醇水平差异均无统计学意义 ($P>0.05$)。3 组间移植胚胎数、移植优质胚胎数及治疗前子宫内膜厚度差异均无统计学意义 ($P>0.05$)。治疗后, 子宫内膜厚度 A 组 [(7.7 ± 0.8) mm] 显著高于 B 组 [(7.3 ± 0.8) mm, $P=0.002$] 和 C 组 [(6.7 ± 0.9) mm, $P<0.001$], B 组显著高于 C 组 ($P<0.001$)。子宫内膜血流: 阻力指数 (RI) 和搏动指数 (PI) A 组 (0.52 ± 0.10 , 1.27 ± 0.21) 低于 B 组 (0.57 ± 0.07 , 1.64 ± 0.41) 和 C 组 (0.68 ± 0.14 , 2.27 ± 0.48), 3 组间差异有统计学意义 ($P<0.001$)。收缩末期与舒张末期血流速度比值 (S/D): C 组 (3.39 ± 0.89) 显著高于 B 组 (2.50 ± 0.46 , $P<0.001$) 和 A 组 (2.37 ± 0.32 , $P<0.001$); A 组和 B 组间差异无统计学意义 ($P>0.05$)。C 组周期取消率 (33.33%) 比 A 组 (13.16%)、B 组 (18.06%) 都高, 3 组间差异有统计学意义 ($P=0.010$)。A 组临床妊娠率 (48.48%) 高于其他两组 (28.81%, 27.27%), 3 组间差异有统计学意义 ($P=0.027$), 但流产率 3 组间差异没有统计学意义 ($P>0.05$)。**结论** 在 FET 周期, 激素替代联合宫腔灌注 GH 治疗可增加子宫内膜厚度、改善薄型子宫内膜下血流状况, 而且操作简单。

【关键词】 生殖技术, 辅助; 薄型子宫内膜; 生长激素

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Clinical research on the application of growth hormone in the preparation of thin endometrium

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【Abstract】 Objective To explore the effectiveness of growth hormone (GH) combined with hormone replacement therapy in thin endometrium patients preparing for frozen-thawed embryo transfer (FET). **Methods** Prospective cohort study was performed. Totally 214 patients who had been treated in Reproductive Center of Jiuzhou Perfect Hospital of Shenyang from January 2017 to June 2019, cancelled fresh cycle transplantation due to endometrial thickness less than 7 mm on the day of human chorionic gonadotropin (hCG) administration in previous fresh cycle, were divided into three groups according to their wishes: group A, hormone replacement combined with intrauterine perfusion of growth hormone ($n=76$); group B, hormone replacement combined with subcutaneous injection of GH ($n=72$); group C, single hormone replacement therapy ($n=66$). The basic situation of patients and prognostic indicators of FET among the three groups were compared. **Results** There was no significant difference in age, infertility duration, body mass index (BMI), basic follicular stimulating hormone (FSH), basic luteinizing hormone (LH) and basic estrogen among the three groups ($P>0.05$). And there was no significant difference in the number of embryos transferred, the number of high-quality embryos transferred and the thickness of endometrium before treatment ($P>0.05$). After treatment, endometrial thickness of group A [(7.7 ± 0.8) mm] was higher than that of group B [(7.3 ± 0.8) mm, $P=0.002$] and group C [(6.7 ± 0.9) mm, $P<0.001$], and that of group B was higher than that of group C ($P<0.001$), the difference was statistically significant. Endometrial blood flow: resistance index (RI) and pulsation index (PI) of group A (0.52 ± 0.10 , 1.27 ± 0.21) were lower than those of group B (0.57 ± 0.07 , 1.64 ± 0.41) and group C (0.68 ± 0.14 , 2.27 ± 0.48), and the difference among the three groups was statistically significant ($P<0.001$). Ratio of end systolic to end diastolic velocity (S/D) of group C (3.39 ± 0.89) was higher than that of group B (2.50 ± 0.46 , $P<0.001$) and group A (2.37 ± 0.32 , $P<0.001$), but there was no significant difference between group A and group B ($P>0.05$). The cancellation rate of cycle in group C (33.33%) was higher than that in group A (13.16%) and group B (18.06%), and the pregnancy rate in group A (48.48%) was higher than that in groups B and C (28.81%, 27.27%), the differences were statistically significant among the three groups ($P=0.010$, $P=0.027$). But there was no significant difference in abortion rate among the three groups ($P>0.05$). **Conclusion** In FET cycle, hormone replacement combined with GH intrauterine perfusion can increase endometrial thickness, improve thin endometrial blood flow, and the operation is simple.

【Key words】 Reproductive technology, assisted; Thin endometrium; Growth hormone

Fund program: Science and Technology Project of Liaoning (2017225081); Shenyang Science and Technology Bureau Planned Projects (18-014-4-55)

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腹腔镜下暂时阻断髂内动脉在子宫瘢痕妊娠中的临床研究

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【摘要】 目的 探讨腹腔镜下双侧髂内动脉暂时性阻断下行剖宫产瘢痕妊娠病灶清除术+修补术的临床研究。方法 回顾性研究 2017 年 2 月至 2018 年 10 月期间河南省人民医院妇科收治剖宫产瘢痕部位妊娠患者 60 例, 其中 A 组 30 例, II~III 型子宫瘢痕妊娠患者选用腹腔镜下双侧髂内动脉暂时性阻断下行剖宫产瘢痕部位病灶清除术+修补术治疗, B 组 30 例, 选用传统介入子宫动脉栓塞术后+清宫术治疗, 比较两组患者出血量、住院时间、住院费用、术后月经复潮时间及再次妊娠结局等情况。结果 A 组手术出血量 [(38.5±22.0) mL]、住院时间 [(4.2±1.5) d]、住院费用 [(21 720±685) 元] 与 B 组 [(100.0±25.0) mL、(5.6±2.2) d、(28 756±980) 元] 比较, 差异有统计学意义 ($P=0.006$ 、 0.008 、 0.019)。两组术后血人绒毛膜促性腺激素 (hCG) 下降率、月经恢复时间等相比较, 差异均无统计学意义 ($P>0.05$)。结论 腹腔镜下双侧髂内动脉暂时性阻断下行剖宫产瘢痕部位病灶清除术+修补术治疗剖宫产妊娠优于传统介入子宫动脉栓塞术后+清宫术, 疗效确切、手术创伤小、相比较介入治疗手术费用较低等优点, 提高术后再次妊娠率及分娩率、降低再次瘢痕妊娠率, 是治疗子宫瘢痕妊娠的较理想方法, 值得临床推广。

【关键词】 子宫瘢痕妊娠; 腹腔镜; 髂内动脉阻断; 清宫术

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Clinical study of laparoscopic temporary occlusion of internal iliac artery in uterine scar pregnancy

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【Abstract】 Objective To investigate the therapeutic effect of laparoscopic bilateral internal iliac artery temporary occlusion on cesarean section scar pregnancy. **Methods** Retrospective research was performed in 60 cases of cesarean scar pregnancy who were treated in Gynecology Department of Henan Provincial People's Hospital from February 2017 to October 2018. Among them, 30 cases in group A were treated by type II-III of laparoscopic bilateral internal iliac artery temporary occlusion followed by cesarean scar lesion clearance and repair, 30 cases in group B were treated by traditional interventional uterine artery embolization plus clearance. The bleeding volume, hospitalization time, hospitalization expenses, the time of menstruation after operation and the outcome of secondary pregnancy were compared between the two groups. **Results** Group A had less bleeding [(38.5±22.0) mL], shorter hospitalization time [(4.2±1.5) d], less hospitalization expenses [(21 720±685) yuan] compared with group B [(100.0±25.0) mL, (5.6±2.2) d, (28 756±980) yuan], the results were all statistically significant ($P<0.05$). There were no significant differences in the reduction rate of human chorionic gonadotrophin (hCG) and the recovery time of menstruation between the two groups ($P>0.05$). **Conclusion** Laparoscopic excision and repair of scar site of cesarean section under temporary bilateral internal iliac artery occlusion is superior to traditional interventional uterine artery embolization plus uterine curettage in the treatment of cesarean section pregnancy. It has the advantages of exact curative effect, less surgical trauma and lower cost compared with interventional therapy. It can improve the rate of re-pregnancy after operation. It is an ideal method to treat uterine scar pregnancy by improving the rate of secondary pregnancy, delivery rate of secondary pregnancy and reducing the rate of secondary scar pregnancy. It can improve the treatment level of scar pregnancy and is worth popularizing.

【Key words】 Cesarean scar pregnancy; Laparoscopic; Internal iliac artery occlusion curettage; Uterine curettage

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子宫内膜异位症患者腹腔液和肿瘤坏死因子 $-\alpha$ 对颗粒细胞功能和自噬的影响

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【摘要】 目的 研究腹膜型 I~II 期子宫内膜异位症 (endometriosis, EMS) 患者腹腔液与肿瘤坏死因子 $-\alpha$ (tumor necrosis factor- α , TNF- α) 对体外培养的颗粒细胞的功能和自噬的影响, 从而探讨腹膜型 EMS 的不孕原因。方法 体外培养人卵巢颗粒细胞系 KGN, 分别加入 EMS 患者腹腔液 (EMS 组) 和重组 TNF- α 蛋白 (浓度分别为 1 $\mu\text{g/L}$ 、10 $\mu\text{g/L}$ 、100 $\mu\text{g/L}$) (TNF- α 组) 处理细胞, 以非 EMS 患者腹腔液作对照组。采用 CCK-8 法检测细胞增殖水平, 流式细胞术和线粒体膜电位检测细胞凋亡, 酶联免疫吸附试验 (ELISA) 检测培养液雌二醇和孕酮水平, 蛋白质印迹法检测自噬标志物 LC3-II、LC3-I 和 p62, 透射电子显微镜观察自噬小体数量。结果 加入 EMS 患者腹腔液可抑制 KGN 颗粒细胞增殖 ($P < 0.001$), 促进颗粒细胞凋亡 ($P = 0.009$), 减少雌、孕激素的分泌 ($P < 0.001$, $P = 0.005$); EMS 患者腹腔液和高浓度重组 TNF- α 蛋白可促进颗粒细胞自噬标志物 LC3-II/LC3-I 比值上升 ($P < 0.001$), p62 蛋白减少 ($P < 0.05$), 自噬体数量增加 ($P < 0.001$), 自噬过度激活。结论 EMS 患者腹腔液和 TNF- α 通过抑制卵巢颗粒细胞增殖、促进凋亡, 影响雌、孕激素的分泌和过度自噬等多个环节影响颗粒细胞的功能, 进而可能通过颗粒细胞的旁分泌和自分泌功能影响卵子质量、受精及随后的胚胎发育和胚胎着床, 从而导致 EMS 患者不孕。

【关键词】 子宫内膜异位症; 腹腔液; 肿瘤坏死因子 $-\alpha$; 颗粒细胞; 自噬

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Effects of peritoneal fluid and tumor necrosis factor- α on granulosa cell function and autophagy in endometriosis patients

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【Abstract】 Objective To investigate the effects of peritoneal fluid of peritoneal type I–II endometriosis (EMS) patients and tumor necrosis factor- α (TNF- α) on granulosa cells function and autophagy, and to investigate the causes of infertility in peritoneal endometriosis. **Methods** Human ovarian granulosa cell line KGN was cultured *in vitro*, and cells were treated with peritoneal fluid of EMS patients (EMS group) and recombinant TNF- α protein in different concentrations (1 $\mu\text{g/L}$, 10 $\mu\text{g/L}$, 100 $\mu\text{g/L}$) (TNF- α group), respectively. Peritoneal fluid of non-EMS patients served as control group. Cell proliferation was detected by CCK-8 method, cell apoptosis was detected by flow cytometry and mitochondrial membrane potential, estradiol and progesterone levels were detected by enzyme-linked immunosorbent assay (ELISA), and autophagic markers including LC3-II/LC3-I and p62 were detected by Western blotting. The number of autophagosomes was observed by transmission electron microscopy. **Results** EMS patients' peritoneal fluid and high concentrations of recombinant TNF- α protein inhibited KGN granulosa cell proliferation ($P < 0.001$), promoted granulosa cell apoptosis ($P = 0.009$), and decreased estradiol and progesterone secretion levels ($P < 0.001$, $P = 0.05$), promoted granulocyte autophagy markers LC3-II/LC3-I ratio increased ($P < 0.001$), the p62 protein decreased ($P < 0.05$), the number of autophagosomes increased ($P < 0.001$), and autophagy was over activated. **Conclusion** EMS patients' peritoneal fluid and TNF- α can affect the function of granulosa cells by inhibiting the proliferation, promoting apoptosis, affecting the secretion of estradiol and progesterone, and causing excessive autophagy. The paracrine and autocrine functions of granulosa cells may affect oocyte quality, fertilization and embryo development and implantation, resulting in infertility in EMS patients.

【Key words】 Endometriosis; Peritoneal fluid; Tumor necrosis factor- α ; Granulosa cell; Autophagy

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子宫肌瘤组织中长链非编码 RNA 表达谱分析

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【摘要】目的 分析子宫肌瘤组织与正常子宫肌层组织中长链非编码 RNA(long noncoding RNA, lncRNA) 表达谱的差异性, 探讨 lncRNA 在子宫肌瘤发病机制中的作用。**方法** 收集 2017 年 4 月至 2018 年 9 月期间在河南省人民医院因子宫肌瘤行子宫切除术的 41 例患者组织标本。① 通过 SBC-ceRNA 基因芯片技术在 5 例子宫肌瘤组织与配对正常子宫肌层组织中构建差异性 lncRNA 表达谱; ② GO、KEGG 富集分析子宫肌瘤组织中差异表达 lncRNA 的生物学功能及其调控的信号通路; ③ qRT-PCR 方法在 36 例子宫肌瘤组织和正常子宫肌层组织中验证候选 lncRNA 表达的差异性; ④ 结合患者临床病例资料, 分析差异表达 lncRNA 与患者临床病理参数间的相关性。**结果** ① 与子宫肌层组织相比较, 789 条 lncRNAs 在子宫肌瘤组织中的表达水平差异有统计学意义 [差异倍数 ≥ 2 , P 均 < 0.05], 其中 412 条 lncRNAs 在子宫肌瘤组织中表达上调, 377 条 lncRNAs 在子宫肌瘤组织中表达下调。② GO、KEGG 富集分析显示, 子宫肌瘤组织中差异表达 lncRNAs 主要调控的生物学功能及信号通路为细胞外基质积聚及受体相互作用、成纤维细胞生长因子调控、纤维粘连蛋白结合、细胞黏附分子、内皮细胞趋化性、p53 信号通路等。③ qRT-PCR 结果显示, 与正常子宫肌层组织相比较, *RP11-595O22.1*、*CTD-3080F16.3*、*RP11-486F17.1*、*IGF2-AS* 在肌瘤组织中呈现高表达 ($P=0.000\ 3$, $P=0.001\ 1$, $P=0.000\ 2$, $P<0.000\ 1$), *RP11-253M7.1*、*RP11-1100L3.8* 在肌瘤组织中呈现低表达 ($P=0.000\ 6$, $P=0.011$), 提示 qRT-PCR 验证结果与基因芯片表达一致; ④ *IGF2-AS* 在肌瘤组织中的表达水平与肌瘤大小密切相关, 肌瘤直径 > 5 cm 患者 *IGF2-AS* 的表达水平较肌瘤直径 ≤ 5 cm 患者显著升高 ($P=0.043\ 1$)。**结论** 子宫肌瘤组织与正常子宫肌层组织中 lncRNA 的表达水平差异有统计学意义, 成功筛选出子宫肌瘤组织中特异性表达的 lncRNAs, 为研究子宫肌瘤的发病机制及特异性分子标志物和基因靶向治疗提供理论基础。

【关键词】 子宫肌瘤; 长链非编码 RNA; 基因芯片

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Expression profiling of long noncoding RNA in human uterine leiomyoma

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【Abstract】 Objective To investigate the differential expression profiles of long non-coding RNA (lncRNA) in uterine leiomyoma (ULM) and adjacent normal myometrium tissues, explore the role of lncRNA in the pathogenesis of uterine leiomyoma. **Methods** Tissue samples of 41 patients with ULM who underwent hysterectomy in Henan People's Hospital from April 2017 to September 2018 were collected. 1) SBC-ccRNA high throughput microarray technology was performed to identify the differential expression profiles of lncRNA in five ULM tissues and paired normal myometrial tissues. 2) Bioinformatics methods (GO and KEGG) were used to analyze the biological function and regulatory signaling pathway network of the differentially expressed lncRNAs in ULM. 3) qRT-PCR assay was applied to verify the differential expression of candidate lncRNAs in 36 pairs of leiomyoma tissues and paired myometrium tissues. 4) Association of candidate lncRNA expression and clinical pathological features of ULM was evaluated. **Results** 1) A total of 789 differentially expressed lncRNA transcripts (412 up-regulated and 377 down-regulated) were identified between leiomyoma and adjacent myometrium tissues. 2) Enrichment analysis revealed that dysregulated transcripts were mainly involved in extracellular matrix (ECM) assembly, p53 and mTOR signaling transduction. 3) Candidate lncRNAs were selected for validation using qRT-PCR assay in extended clinical samples and demonstrated that *RP11-595O22.1*, *CTD-3080F16.3*, *RP11-486F17.1*, *IGF2-AS* were up-regulated in leiomyoma tissues ($P=0.000\ 3$, $P=0.001\ 1$, $P=0.000\ 2$, $P<0.000\ 1$), whereas *RP11-253M7.1*, *RP11-1100L3.8* were down-regulated ($P=0.000\ 6$, $P=0.011$). 4) Furthermore, *IGF2-AS* levels were associated with leiomyoma size ($P=0.043\ 1$). **Conclusion** LncRNA profiles were identified and differential expression pattern conformed in ULM and paired normal myometrium counterpart. Our study provided an integrated analysis of global lncRNA profile and specific regulatory network in ULM, may give novel epigenetic insight and biomarker for further target therapy development.

【Key words】 Uterine Leiomyoma; Long noncoding RNA; Microarray

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不同多囊卵巢综合征大鼠模型表型及肠道菌群组成差异性研究

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【摘要】 目的 探索更为合适多囊卵巢综合征 (polycystic ovary syndrome, PCOS) 动物造模方法, 并以大鼠肠道菌群探究肠道微生物在不同动物模型中的差异及作用机制。方法 本研究采用 30 只 6 周龄雌性 Sprague Dawley 大鼠, 随机分为对照组、脱氢表雄酮 (DHEA) 组、DHEA+ 光照组 3 组, 每组 10 只大鼠。对照组大鼠每日皮下注射 0.2 mL 磷酸盐缓冲液 (PBS) 溶液, DHEA 组大鼠每日皮下注射等剂量 DHEA 建立 PCOS 大鼠模型, 对照组及 DHEA 组大鼠均饲养于 12 h 光照 /12 h 黑暗环境中; DHEA+ 光照组大鼠除注射等剂量 DHEA 溶液外, 每日暴露于 24 h 光照环境中。经过 4 周处理后, 检测各组大鼠动情周期、卵巢质量及形态学变化、空腹血糖水平; 利用 16S rRNA 测序技术检测大鼠肠道菌群变化情况。**结果** 经过 4 周处理, DHEA 组大鼠出现动情周期紊乱、卵巢重量降低、卵巢多囊样改变等类 PCOS 样表现; 持续光照后, DHEA+ 光照组大鼠同样出现类 PCOS 表现, 同时空腹血糖水平比对照组、DHEA 组大鼠明显升高 ($P < 0.001$)。DHEA+ 光照组大鼠肠道菌群组成异于 DHEA 组, 葡萄球菌 (*Staphylococcus*)、*Jeotgalicoccus*、毛螺菌 (*Lachnospiraceae incertae sedis*) 在 DHEA+ 光照组大鼠肠道中明显富集, 异普氏菌 (*Alloprevotella*)、考拉杆菌 (*Phascolarctobacterium*) 含量大幅降低。功能预测提示差异显著的肠道菌群与多个 PCOS 可能糖代谢通路相关。**结论** 注射 DHEA 同时持续光照可引起大鼠生殖、代谢方面类 PCOS 改变, 与 PCOS 患者临床表现更为相符, 是一种更合适的 PCOS 动物造模方式。肠道菌群在 PCOS 患者糖代谢相关病理生理改变方面可能发挥一定作用。

【关键词】 多囊卵巢综合征; 模型, 动物; 脱氢表雄酮; 持续光照; 肠道菌群

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Differences of manifestation and gut microbiota composition between different polycystic ovary syndrome rat models

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【Abstract】 Objective To explore a more appropriate animal modeling method of polycystic ovary syndrome (PCOS) model, and clarify the variance and mechanism of gut microbiota in PCOS models. **Methods** Totally 30 female Sprague Dawley rats were involved in this study. They were randomly divided into control group, dehydroepiandrosterone (DHEA) group and DHEA+light group, respectively, with 10 rats in each group. Subcutaneous injection of 0.2 mL DHEA was adopted to establish PCOS rat models and 0.2 mL PBS was injected in control group rats. Rats of control group and DHEA group were under 12 h/12 h light/dark exposure. Rats of DHEA+light group were injected with equivalent volume of DHEA and under 24 h continuous light exposure. After treatment for 4 weeks, the estrous cycle, ovarian weight, morphological changes and fasting blood glucose were detected. Gut microbiota of rats was explored with 16S rRNA sequencing technique. **Results** After treatment for 4 weeks, rats in DHEA group had disordered estrous cycles, reduced ovarian weight and polycystic ovaries. Apart from PCOS-like manifestations in DHEA, rats of DHEA+light group had increased fasting blood glucose level ($P<0.001$). The composition of gut microbiota was different between DHEA group and DHEA+light group. In genus level, *Straphylococcus*, *Jeotgalicoccus* and *Lachnospiracea incertae sedis* were enriched in DHEA+light group while the abundance of *Alloprevotella* and *Phascolarctobacterium* were decreased compared with DHEA group. Prediction function analysis implied that there might be association between altered microbial taxa and glucose metabolic pathway in PCOS. **Conclusion** DHEA injection with continuous light exposure induced reproductive and metabolic changes in rats, which were closely similar with the manifestation of PCOS patients. It is a more suitable method to induce PCOS animal model. It is possible that gut microbiota might play a role in the process of glucose metabolic impairment induced by continuous light.

【Key words】 Polycystic ovary syndrome; Models, animal; Dehydroepiandrosterone; Continuous light; Gut microbiota

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受精过程中不同激活力强度对小鼠卵子线粒体三磷酸腺苷和活性氧生成的影响

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【摘要】 目的 通过对三磷酸腺苷 (ATP) 含量及活性氧 (ROS) 水平的检测, 观察在小鼠卵子受精过程中不同水平的激活强度对卵子线粒体代谢的影响。方法 采用我们已经建立的弱激活力小鼠精子对卵子进行卵胞质内单精子显微注射 (ICSI) 后, 施以不同浓度的离子霉素 ($0 \mu\text{mol/L}$ 、 $2.5 \mu\text{mol/L}$ 、 $10 \mu\text{mol/L}$) 处理 10 min 进行辅助激活, 并以正常小鼠精子 ICSI 作为对照。根据处理方式分为 4 组: 正常精子组 (normal, N 组)、激活力减弱精子 (weak sperm, W 组)、激活力减弱精子施以适度辅助激活剂组 (weak sperm+moderate AOA, M 组)、激活力减弱精子施以过度辅助激活剂组 (weak sperm+excessive AOA, E 组)。在 ICSI 后 1.5~2 h 内对卵子内 ATP 含量和 ROS 的水平进行检测。对未进行 ICSI 卵子组 (oocyte, O 组) 进行 ATP 检测。结果 ① ATP 含量检测显示: 随着激活力的上升, O 组 [2.005 ± 0.053 pmol]、W 组 [2.485 ± 0.064 pmol]、M 组 [3.763 ± 0.075 pmol] 的卵子内平均 ATP 含量逐步提高, 且差异有统计学意义 ($P < 0.0001$); 其中 M 组与 N 组 [3.573 ± 0.068 pmol] 平均 ATP 含量接近 ($P > 0.05$); E 组虽较 O 组 [3.204 ± 0.070 pmol] 高, 但其卵子的平均 ATP 含量显著小于 N 组 ($P < 0.001$)。② ROS 水平检测显示: 随着激活力的增加, W 组 (0.420 ± 0.028 , $n=9$)、M 组 (1.097 ± 0.037 , $n=9$)、E 组 (1.361 ± 0.033 , $n=10$) 表现出 ROS 水平的逐步升高 ($P < 0.001$), 其中 M 组与 N 组 ROS 水平 (1.000 ± 0.026 , $n=10$) 也比较接近, 差异有统计学意义 ($P=0.044$)。结论 受精过程中激活力水平将对卵子线粒体代谢产生明显影响, 对弱激活力小鼠精子显微受精后, 行适度激活时, ATP 产量增加, ROS 生成较少; 而过高的激活强度反而会引起 ATP 产量的下降和 ROS 生成的增多。

【关键词】 受精; 卵胞质内单精子注射; 活性氧; 三磷酸腺苷; 辅助激活

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Effects of different activation intensities on mitochondrial adenosine triphosphate and reactive oxygen species production in mouse oocytes during fertilization

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【Abstract】 Objective To observe the effect of different levels of activation intensity on mitochondrial metabolism in mouse oocyte during fertilization by detecting adenosine triphosphate (ATP) content and reactive oxygen species (ROS) level. **Methods** After intracytoplasmic sperm injection (ICSI) with weak sperm, different concentrations of ionomycin (0 $\mu\text{mol/L}$, 2.5 $\mu\text{mol/L}$, 10 $\mu\text{mol/L}$) were applied for 10 min to assist the oocyte activation, and ICSI with normal mouse sperm was used as the control. According to the treatment methods, they were divided into four groups: normal sperm group (normal, N group), weak sperm group (W group), weak sperm + moderate AOA group (M group), weak sperm + excessive assisted oocyte activation (AOA) group (E group). ATP and ROS levels in oocyte were measured within 1.5–2 h after ICSI. In addition, ATP level of oocyte groups (O group) without ICSI was detected. **Results** 1) With the increase of activation power, the average ATP content in oocyte of O group [(2.005 \pm 0.053) pmol], W group [(2.485 \pm 0.064) pmol], M group [(3.763 \pm 0.075) pmol] gradually increased, with a significant difference ($P<0.0001$); the average ATP content in M group was close to that in N group [(3.573 \pm 0.068) pmol] ($P>0.05$). In addition, the average ATP content of eggs in E group [(3.204 \pm 0.070) pmol] was significantly lower than that in N group ($P<0.001$), although it was higher than that in O group. 2) The level of ROS showed that with the increase of activation power, the levels of ROS in W group (0.420 \pm 0.028, $n=9$), M group (1.097 \pm 0.037, $n=9$), E group (1.361 \pm 0.033, $n=10$) increased gradually ($P<0.001$), and the level of ROS in M group only showed slight difference with that of N group (1.000 \pm 0.026, $n=10$) ($P=0.044$). **Conclusion** This study preliminarily found that the level of activation power during fertilization will have a significant impact on mitochondrial metabolism of oocyte. In mouse, when oocyte was moderately activated after ICSI with weak activation ability sperm, ATP production will increase, while ROS production will be less; however, excessive activation intensity will lead to the decrease of ATP production and the increase of ROS production.

【Key words】 Fertilization; Intracytoplasmic sperm injection; Reactive oxygen species; Adenosine triphosphate; Assisted oocyte activation

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维生素 D 受体多态性 *Taq-1* 和 *Apa-1* 增加多囊卵巢综合征的易感性

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【摘要】 目的 探索维生素 D 受体 (VDR) 多态性与多囊卵巢综合征 (PCOS) 发病风险的相关性。方法 利用 Pubmed、Embase、Web of Science、Cochrane library 和中国万方数据库, 检索 VDR 多态性与 PCOS 发病风险关联性研究文献, 截止日期为 2018.09.30。用比值比 (OR) 和 95% 可信区间 (95% CI) 评估 VDR 多态性与 PCOS 发病风险的关联性强度。结果 12 个病例-对照研究 (1824 个病例和 1361 个健康对照) 报道了 4 个 VDR 多态性 (*Taq-1*、*Apa-1*、*Bsm-1* 和 *Fok-1*) 与 PCOS 发病风险的关联性。9 篇高质量研究的 Meta 分析结果显示 *Taq-1* 在隐性遗传模型下 [GG 比 (AA+AG)] 固定效应 OR 为 1.42 (95% CI=1.14~1.76), *Apa-1* 在隐性遗传模型下 [CC 比 (AA+AC)] 固定效应 OR 为 1.31 (95% CI=1.07~1.61); Meta 分析未发现 *Bsm-1*、*Fok-1* 多态性与 PCOS 发病风险的关联性。结论 VDR 基因多态性位点 *Taq-1* 和 *Apa-1* 以隐性遗传模型增加 PCOS 发生风险。

【关键词】 多囊卵巢综合征; 维生素 D 受体; 多态性; 关联性研究

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Vitamin D receptor polymorphisms *Taq-1* and *Apa-1* increase the susceptibility for developing polycystic ovary syndrome

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【Abstract】 Objective To explore the association of polymorphisms in the vitamin D receptor (VDR) gene with polycystic ovary syndrome (PCOS) susceptibility. **Methods** Eligible studies about the association of polymorphisms in the *VDR* gene and PCOS susceptibility were collected by searching PubMed, Embase, Web of Science, Cochrane library and Wanfang databases. The odds ratio (*OR*) along with their corresponding 95% confidence interval (*CI*) was used to estimate the strength of associations. **Results** Four polymorphisms in *VDR* gene (*Taq-1*, *Apa-1*, *Bsm-1* and *Fok-1*) were included in this Meta-analysis. Twelve case-control studies (1824 cases and 1361 controls) evaluated the role of four polymorphisms in PCOS risk. The Meta-analysis of nine high-quality studies on *Taq-1* and *Apa-1* found the fixed-effect *OR* reached 1.42 (95% *CI*=1.14–1.76) and 1.31 (95% *CI*=1.07–1.61) in the recessive genetic model, respectively. No association of *Bsm-1* and *Fok-1* polymorphisms with PCOS was found. **Conclusion** This Meta-analysis suggests that *Apa-1* and *Taq-1* contribute to the risk for developing PCOS under recessive genetic model.

【Key words】 Polycystic ovary syndrome; Vitamin D receptor; Polymorphisms; Association study

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子宫腺肌病年轻不孕患者体外受精 / 卵胞质内单精子显微注射妊娠结局分析

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【摘要】目的 分析年龄 <35 岁的子宫腺肌病不孕患者行体外受精 / 卵胞质内单精子显微注射 (IVF/ICSI) 妊娠结局。**方法** 回顾性分析本中心 2014 年 1 月至 2017 年 12 月期间于南京大学医学院附属鼓楼医院生殖医学中心行 IVF/ICSI 治疗并获得临床妊娠的 2651 例患者的妊娠结局。其中, 129 例子宫腺肌病合并不孕症患者作为子宫腺肌病组, 2522 例单纯输卵管因素不孕患者为对照组。**结果** ①两组年龄、不孕年限、体质量指数、基础窦卵泡数、既往生育史比较差异均无统计学意义 ($P>0.05$)。②行 IVF 的人群中, 子宫腺肌病组自然流产率显著高于对照组 (13.79% 比 6.96%, $P=0.009$); 孕周、胎儿体质量、早产率组间比较, 差异均无统计学意义 ($P>0.05$)。行 ICSI 的人群中, 子宫腺肌病组与对照组的自然流产率、孕周、胎儿体质量、早产率组间差异均无统计学意义 ($P>0.05$)。③单胎妊娠的子宫腺肌病组自然流产率高于对照组, 差异有统计学意义 (12.05% 比 6.31%, $P=0.040$)。双胎妊娠组中子宫腺肌病组孕周显著小于对照组 [(35.68±3.35) 周比 (36.72±1.99) 周, $P=0.002$], 单胎妊娠组中子宫腺肌病组的孕周与对照组间差异无统计学意义 ($P>0.05$); 无论单胎妊娠还是双胎妊娠, 胎儿体质量和早产率在子宫腺肌病组和对照组间差异均无统计学意义 ($P>0.05$)。④双胎组中, 子宫腺肌病患者和对照组的孕周、胎儿体质量均显著低于单胎组 ($P<0.000 1$), 早产率显著高于单胎组 ($P<0.000 1$)。**结论** 对于 <35 岁的年轻不孕症患者, 子宫腺肌病明显增加 IVF 自然流产的风险, 但不增加早产和低出生体质量儿的风险。子宫腺肌病患者和单纯输卵管因素不孕患者中, 双胎妊娠均显著增加 IVF/ICSI 早产和低出生体质量儿的风险。

【关键词】 受精, 体外; 胚胎移植; 妊娠结局; 子宫腺肌病

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Study of pregnancy outcomes after *in vitro* fertilization/intracytoplasmic sperm injection in young infertile patients with adenomyosis

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【Abstract】 Objective To analyze the pregnancy outcomes of *in vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI) in infertility patients with adenomyosis aged less than 35 years. **Methods** Retrospective analysis was performed on the pregnancy outcomes of 2651 patients who underwent IVF/ICSI treatment and obtained clinical pregnancy in Reproductive Medicine Center of Nanjing Drum Tower Hospital from January 2014 to December 2017. Among them, adenomyosis group had 129 cases of adenomyosis with infertility patients; control group had 2522 cases of tubal factor infertility patients. **Results** 1) There were no significant differences in age, infertility duration, body mass index, number of basal sinus follicle and past reproductive histories between the two groups ($P>0.05$). 2) In patients undergoing IVF, the spontaneous miscarriage rate in the adenomyosis group was significantly higher than that in control group (13.79% vs. 6.96%, $P=0.009$). There were no significant differences in gestational age, fetal weight, and preterm delivery rate between the two groups ($P>0.05$). In patients undergoing ICSI, there were no significant differences in the spontaneous miscarriage rate, gestational age, fetal weight, and preterm delivery rate between the two groups ($P>0.05$). 3) Single pregnancy group and twin pregnancy group were compared respectively. In single pregnancy patients, the spontaneous miscarriage rate in adenomyosis group was higher than that in control group (12.05% vs. 6.31%, $P=0.040$). In twin pregnancy patients, gestational weeks of patients in adenomyosis group were significantly less than those in control group [(35.68±3.35) weeks vs. (36.72±1.99) weeks, $P=0.002$]. There were no significant differences in gestational age in single pregnancy patients between the two groups ($P>0.05$). There were no statistically significant differences in fetal weight and preterm delivery rates between adenomyosis group and control group, regardless of single or twin pregnancies ($P>0.05$). 4) In twin pregnancy patients, gestational age and fetal weight were significantly lower than those in single pregnancy patients ($P<0.000 1$), and preterm birth rate was significantly higher than that in single pregnancy patients ($P<0.000 1$). **Conclusion** For infertile patients less than 35 years, adenomyosis significantly increases the risk of IVF spontaneous miscarriage, but does not increase the risk of premature birth and low birth weight. Twin pregnancies significantly increased the risk of IVF/ICSI preterm birth and low birth weight in both adenomyosis and tubal infertility.

【Key words】 Fertilization *in vitro*; Embryo transfer; Pregnancy outcome; Adenomyosis

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低级别囊胚冻融移植结局影响因素的相关性分析

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【摘要】 目的 分析影响低级别囊胚冻融移植临床结局的相关因素。方法 回顾性分析 2014 年 3 月至 2018 年 3 月期间在安徽医科大学第一附属医院生殖医学中心行低级别囊胚冻融移植的 358 个周期, 根据移植后 14 d 血人绒毛膜促性腺激素 (hCG) 值及移植后 35 d 阴道超声结果, 分为妊娠组和非妊娠组, 妊娠组 28 个周期, 非妊娠组 330 个周期, 探究影响妊娠结局的原因。结果 ①低级别囊胚冻融移植的妊娠率为 12.01%(43/358), 临床妊娠率为 7.82%(28/358), 生化妊娠率为 4.19%(15/358), 流产率为 21.43%(6/28), 活产率为 6.15%(22/358); ②年龄、女方体质量指数 (BMI)、不孕类型、不孕年限、移植日子宫内膜厚度、移植胚胎数等不影响低级别囊胚移植的临床结局; ③囊胚发育天数影响低级别囊胚的冻融移植结局, 第 5 日 (D5) 囊胚种植率 (26.51%)、临床妊娠率 (26.83%)、活产率 (19.51%) 显著高于第 6 日 (D6) 囊胚 (6.20%、5.36%、4.42%)(P 均 $<0.000 1$)。结论 低级别囊胚冻融移植成功率较低, D5 囊胚比 D6 囊胚具有更高的移植成功率。

【关键词】 低级别胚胎囊胚; 冻融囊胚移植; 妊娠结局; 囊胚

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Correlation analysis of influencing factors of low-grade blastocyst freeze-thaw graft outcome

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【Abstract】 Objective To analyze the factors influencing the clinical outcome of low-grade blastocyst freeze-thaw transplantation. **Methods** Totally 358 cycles of low-grade blastocysts in the Reproductive Medicine Center of the First Affiliated Hospital of Anhui Medical University from March 2014 to March 2018 was retrospectively analyzed. According to the blood human chorionic gonadotropin (hCG) value at 14 d after transplantation and the vaginal ultrasound results at 35 d after transplantation, the patients were divided into pregnancy group ($n=28$) and non-pregnancy group ($n=330$). The reasons influencing pregnancy outcome were explored. **Results** 1) Pregnancy rate of low grade blastocyst freeze-thaw transplantation was 12.01% (43/358), the clinical pregnancy rate was 7.82% (28/358), the biochemical pregnancy rate was 4.19% (15/358), the abortion rate was 21.43% (6/28), and the live birth rate was 6.15% (22/358). 2) Age, female body mass index (BMI), type of infertility, infertility duration, the endometrial thickness of the transplant day, the number of transplanted embryos, etc., did not affect the clinical outcome of low-grade embryo transfer ($P>0.05$). 3) The development days of blastocyst affected the outcome of freeze-thaw transplantation of low-grade blastocyst. Day 5 (D5) blastocyst implantation rate (26.51%), clinical pregnancy rate (26.83%), and live birth rate (19.51%) were significantly higher than those of day 6 (D6) blastocysts (6.20%, 5.36%, 4.42%) ($P<0.000 1$). **Conclusion** The success rate of low grade blastocyst freeze-thaw transplantation is low, and D5 blastocysts have a higher transfer success rate than D6 blastocysts.

【Key words】 Low-grade embryo blastocyst; Freeze-thaw blastocyst transfer; Pregnancy outcome; Blastocyst

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反复种植失败患者生活质量现状及影响因素分析

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【摘要】目的 了解接受体外受精-胚胎移植(IVF-ET)且反复种植失败(repeated implantation failure, RIF)患者生活质量的现状,分析其影响因素,为制定有效的干预措施提供科学依据。**方法** 采用横断面调查研究,选取2018年7月至2018年12月期间在兰州大学第一医院生殖医学专科医院接受IVF-ET的115例RIF患者进行问卷调查,采用患者基本情况调查表、生育生活质量问卷(FertiQoL)和焦虑自评量表(SAS)、抑郁自评量表(SDS)评估RIF患者的焦虑抑郁情绪和生活质量,运用SPSS21.0进行统计分析。**结果** 患者整体生育生活质量评分为 (55.8 ± 16.4) 分,生活质量各领域中治疗耐受性得分最低 $[(48.6 \pm 21.0)$ 分],情感领域位于其次 $[(49.4 \pm 22.5)$ 分],治疗环境领域得分最高 $[(65.1 \pm 13.6)$ 分]。多因素回归分析结果显示,RIF患者生育生活质量的影响因素依次为抑郁情绪、焦虑情绪、辅助生殖助孕失败次数、婚姻史、体质量指数(BMI)、丈夫为独生子。**结论** RIF患者生活质量受到严重影响,焦虑情绪、抑郁情绪、辅助生殖助孕失败次数、婚姻史、BMI、丈夫为独生子等是其主要影响因素。

【关键词】 受精, 体外; 反复种植失败; 生活质量; 影响因素分析

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Analysis of current quality of life and influencing factors of patients with repeated implant failure

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【Abstract】 Objective To understand the status quo of quality of life in patients undergoing *in vitro* fertilization-embryo transfer (IVF-ET) with repeated implantation failure (RIF), and to analyze its influencing factors, and provide a scientific basis for developing effective interventions and RIF. **Methods** A cross-sectional survey was conducted to investigate 115 patients with RIF who underwent IVF-ET at the Reproductive Medicine Special Hospital of the 1st hospital of Lanzhou University from July 2018 to December 2018. The patient's basic situation questionnaire, fertility quality of life questionnaire (FertiQoL) and anxiety self-rating scale (SAS), depression self-rating scale (SDS) were used to evaluate the anxiety, depression and quality of life of patients with RIF. Statistical analysis was performed using SPSS21.0. **Results** The overall reproductive quality of life score was 55.8 ± 16.4 , the lowest was in the therapeutic tolerance (48.6 ± 21.0), the emotional field was the second (49.4 ± 22.5), and the highest was in the therapeutic environment (65.1 ± 13.6). Multivariate regression analysis showed that the factors influencing the quality of life of RIF patients were depression, anxiety, number of assisted reproductive failures, marriage history, body mass index (BMI), and husband as the only child. **Conclusion** The quality of life of patients with RIF is severely affected. Anxiety, depression, number of assisted reproductive failures, marriage history, BMI, and husband as the only child are the main influencing factors.

【Key words】 Fertilization *in vitro*; Repeated implantation failure; Quality of life; Root cause analysis

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人文关怀对失独患者行辅助生殖治疗过程中心理状态、诊疗体验及妊娠结局的影响

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【摘要】 **目的** 探讨人文关怀对失独患者行辅助生殖治疗过程中心理状态、诊疗体验以及辅助生殖结局的影响。**方法** 按照初次就诊顺序, 采用随机数字表法, 选取 2016 年 3 月至 2018 年 11 月期间在南京医科大学第二附属医院生殖医学科门诊接受辅助生殖治疗的女性失独患者 89 例分为对照组 ($n=44$): 按照辅助生殖正常诊疗过程进行常规护理和宣教; 人文关怀组 ($n=45$): 根据失独患者特殊经历和心理, 进行以人文关怀为主的优质诊疗服务, 包括心理方面的疏导和关怀、社会支持系统的搭建、多元化的宣教、认知与行为指导、手术过程的人性化安排。了解两组患者在接受辅助生殖治疗前后的心理状态、患者对就诊过程的满意度评分以及辅助生殖相关结局。**结果** 治疗结束后人文关怀组患者焦虑状态、抑郁状态评分以及生育生活质量中情感、身心、社会关系、治疗环境各项评分均显著优于对照组和治疗前, 差异均有统计学意义 ($P<0.05$); 人文关怀组患者治疗耐受性评分 (71.0 ± 6.2) 显著高于对照组 (67.0 ± 5.4), 差异有统计学意义 ($P=0.039$), 但与治疗前 (68.0 ± 6.6) 比较, 差异无统计学意义 ($P=0.342$); 人文关怀组治疗后, 婚姻评分 (62.4 ± 7.4) 与治疗前 (61.0 ± 6.8) 和对照组 (64.7 ± 9.1) 间, 差异均无统计学意义 ($P=0.634$, $P=0.131$)。人文关怀组患者就诊满意度评分 (34.5 ± 2.1) 显著高于对照组 (31.5 ± 2.0), 差异有统计学意义 ($P<0.001$)。人文关怀组的获卵数、种植率、临床妊娠率略高于对照组, 但差异均无统计学意义 ($P>0.05$), 两组患者的流产率差异无统计学意义 ($P=0.831$)。**结论** 辅助生殖诊疗过程中的人文关怀可以有效改善失独患者就诊过程中的焦虑、抑郁状态并提高生育生活质量, 改善就诊体验, 提高失独患者就诊满意度, 一定程度上可改善其辅助生殖治疗结局。

【关键词】 人文关怀; 失独者; 不孕症; 辅助生殖

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Effect of humanistic care on psychological status, experience of diagnosis and treatment and pregnancy outcomes in assisted reproductive therapy to the only-child-lost patients

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【Abstract】 Objective To investigate the effect of humanistic care on psychological status, experience of diagnosis and treatment and pregnancy outcomes in assisted reproductive therapy to the only-child-lost patients. **Methods** A total of 89 cases of the only-child-lost patients treated in the outpatient department of Reproductive Medicine Department, the Second Affiliated Hospital of Nanjing Medical University from March 2016 to November 2018 were divided into control group ($n=44$) and humanistic care group ($n=45$) according to the order of the initial visits of patients, with the method of the random number table. Control group received routine nursing and healthy education, while the humanistic care group accepted high-quality diagnosis and treatment service mainly based on humanistic care, including psychological counseling and care, construction of social support system, diversified propaganda, cognitive and behavioral guidance, and humanized arrangement of operation process, according to the special experience and psychology of the only-child-lost patients. The psychological status before and after assisted reproductive technology, the satisfaction score of patients in the process of consultation and pregnancy outcomes were compared between the two groups. **Results** After therapy, the anxiety score, depression score and the score of emotion, mind/body, relational and social, treatment environment of fertility-related quality of life were significantly better among patients in humanistic care group than in control group and those before treatment ($P<0.05$). The score of treatment tolerance of fertility-related quality of life was significantly higher in humanistic care group (71.0 ± 6.2) than in control group (67.0 ± 5.4) ($P=0.039$), while there was no significant difference between before (68.0 ± 6.6) and after treatment ($P=0.342$). No significant differences were identified considering the score of marriage in intra-group ($P=0.634$, $P=0.131$) and inter-group ($P=0.131$). The satisfaction score of patients in humanistic care group (34.5 ± 2.1) was higher than that in control group (31.5 ± 2.0) with significant differences ($P<0.001$). The number of retrieved oocytes, the implantation rate and the clinical pregnancy rate were slightly higher in treatment group than in control group, but no significant differences were identified ($P>0.05$). There was no significant difference in miscarriage rate between the two groups ($P=0.831$). **Conclusion** Humanistic care in assisted reproductive diagnosis and treatment could effectively decrease the anxiety and depression status, improve treatment-related fertility quality of life, improve the experience of consultation, improve the satisfaction of the only-child-lost patients, and might

胚胎植入前非整倍体遗传学筛查对改善男性因素不孕夫妇 辅助生殖结局的研究进展

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【摘要】 自胚胎植入前非整倍体遗传学筛查 (preimplantation genetic testing for aneuploidies, PGT-A) 技术开展以来, 越来越多的不孕不育患者接受了这一治疗成功生育健康子代。PGT-A 技术是通过遗传学手段对体外授精得到的胚胎进行染色体检测, 从而达到筛选出染色体整倍体胚胎进行移植的目的。目前 PGT-A 主要用于女性高龄、反复流产或反复的胚胎种植失败。近年来, PGT-A 也被推荐用于男性因素所致不孕不育的患者中。但 PGT-A 对男性因素不孕夫妇的辅助生殖治疗结局的改善作用, 仍是学界探讨和研究的一个问题。本文综述了 PGT-A 与男性不育相关的研究进展, 探讨 PGT-A 技术对男性因素不孕夫妇辅助生殖结局的改善作用。

【关键词】 生殖技术, 辅助; 非整倍性; 胚胎植入前非整倍体遗传学筛查; 男性不育

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Role of preimplantation genetic testing for aneuploidies in male factor infertility

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【Abstract】 Nowadays, more and more infertility couples have benefited from preimplantation genetic testing for aneuploidies (PGT-A). PGT-A is a technique that has used genetic technology to examine chromosomes in embryos from couples undergoing *in vitro* fertilization with the aim of helping select the normal chromosome embryo for transfer. PGT-A is mostly used for advanced maternal age, repeated miscarriage and repeated implantation failure. While for now male factor infertility, particularly severe oligoasthenozoospermia or severe teratozoospermia, is also regarded as one of the indications, it's still controversial whether PGT-A could provide noteworthy aids for these patients. In this review, the effects of PGT-A on clinical outcomes of the patients who are involved in male factor infertilities are reviewed.

【Key words】 Reproductive technology, assisted; Aneuploidy; Preimplantation genetic testing for aneuploidy; Male infertility

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男性生殖道人乳头瘤病毒感染对生育力和胚胎发育的影响及其预防

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周梁和潘峰对本文有同等贡献

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【摘要】 人乳头瘤病毒 (HPV) 是最常见的性传播病毒之一, 对男性和女性的生育能力都会产生严重影响。最近研究表明, HPV 感染可能对男性生育能力产生不利影响, 包括精子活力、形态、精子 DNA 完整性和其他精液参数。感染 HPV 的精子可能起到了载体作用, 将 HPV 转移到卵母细胞内。HPV 感染的男性可以将病毒传播给女性伴侣, 导致宫内 HPV 感染, 进而影响胚胎发育, 并降低妊娠率或导致流产。值得注意的是, 精子库的冻存精子亦有 HPV 感染风险。HPV 疫苗可在一定程度上降低宫颈癌、阴茎癌或生殖器疣的发病率。令人信服的数据表明, 男性包皮环切术有助降低男性和女性的生殖道 HPV 感染, 这为降低宫颈癌、阴茎癌的发病率和多种相关的性传播疾病提供了巨大的益处, 又被称为“外科疫苗”。在这篇综述中, 我们强调了男性 HPV 感染的预防和治疗, 包括男性生育能力, 女性生殖健康和子代安全性。本文从男性 HPV 感染的预防和治疗, 包括男性生育能力, 女性生殖健康和子代安全性进行综述。

【关键词】 人乳头瘤病毒感染; 男性生育力; 胚胎发育; 包皮环切; 生殖健康

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Effects of human papilloma virus infection in the male reproductive tract on fertility and embryonic development and its prevention

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【Abstract】 Human papillomavirus (HPV) is one of the most common sexually transmitted viruses that can have some serious impacts to fertility for both men and women. Recent studies showed that HPV infection may have adverse effects on male fertility with sperm motility, morphology, sperm DNA integrity and other semen parameters. Sperm may act as a carrier and transfer HPV to the oocyte. In addition, male with infected can transmit the virus to female partners, causing intrauterine HPV infection that can potentially affect embryonic development, and reduce the pregnancy rate or result to miscarriage. Notably, sperm with risk of HPV infected should be aware in routing sperm bank practice. HPV vaccine may reduce the incidence of cervical cancer, penile cancer or genital warts in a certain extent. Compelling data indicated that male circumcision reduces HPV in men and women, which provides great benefits of reduction and prevention of cervical cancer, penile cancer and a variety of sexually transmitted diseases, known as the 'surgical vaccine'. In this review, we emphasized the prevention and treatment of male HPV infection for male fertility, female reproductive health and the safety of offspring. In this review, we discussed the prevention and treatment of male HPV infection, especially for male fertility, female reproductive health and the safety of offspring.

【Key words】 Human papillomavirus infection; Male fertility; Embryo development; Male circumcision; Reproductive health

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子宫内膜异位症相关 microRNAs 的研究进展

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【摘要】 子宫内膜异位症 (endometriosis, EMS) 是一种雌激素依赖型的慢性炎症性妇科常见疾病, 临床上目前尚缺乏有效的诊治手段。MicroRNAs(miRNAs) 是一类小分子非编码 RNA, 参与调控靶基因的表达, 与人类疾病的病理过程相关, 且能在外周血中稳定存在, 是理想的疾病生物标志分子。为了探讨 miRNAs 在 EMS 病理过程中的作用, 已有许多研究利用高通量技术, 分别从 EMS 患者的异位内膜组织、子宫内膜间质和上皮细胞, 以及外周血中, 筛选到一批存在差异表达的 EMS 相关 miRNAs。本文将对 EMS 相关 miRNAs 的鉴别及其作为 EMS 生物标志分子的研究进展进行综述, 以期从事相关研究和临床工作的专业人员提供参考。

【关键词】 子宫内膜异位症; MicroRNAs; 在位内膜组织; 异位内膜组织; 生物标志分子

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Recent insights on the endometriosis-associated microRNAs

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【Abstract】 Endometriosis (EMS) is an estrogen-dependent chronic inflammatory gynecologic disorder, and the clinical intervention measures of EMS are still needed to be improved at present. MicroRNAs (miRNAs) are small non-coding RNA that modulate gene expression and participate in the pathogenesis of various human diseases. Stability of miRNAs in peripheral blood makes them as attractive candidate biomarkers. In order to explore roles of miRNAs in the EMS pathogenesis, eutopic endometrial tissues and ectopic endometrial tissues, and their isolated stromal and epithelial cell, as well as peripheral blood samples have been used to indentify EMS-associated miRNAs by high-throughput techniques, and a number of dysregulated miRNAs have been reported. This review aims to provide recent insights on these reported EMS-associated miRNAs with a special emphasis to their potential application as biomarkers for EMS.

【Key words】 Endometriosis; MicroRNAs; Eutopic endometrial tissues; Ectopic endometrial tissues; Biomarkers

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