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专栏导读——辅助生殖技术提高配子胚胎质量、优化评估体系、改善临床结局系列研究

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【摘要】 在辅助生殖治疗过程中，如何通过有效的临床及实验室干预帮助患者获得更佳质量的配子及胚胎是重要问题。本专栏通过数篇文献探讨不同促排卵方案对卵母细胞质量的影响，促排卵过程中添加辅助药物对卵母细胞及胚胎质量的影响，临床策略管理对临床结局的影响，以及配子及胚胎质量评估新方法，并对基础和临床研究现状以及疾病诊疗策略进行展示。

【关键词】 配子； 胚胎； 质量管理； 临床结局

Special column reading guide: serial researches on assisted reproductive technology enhancing gamete embryo quality, optimizing evaluation system and improving clinical outcome

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【Abstract】 In the process of assisted reproductive technology (ART), how to help patients get better quality gametes and embryos through effective clinical and laboratory interventions is an important issue. This column reviews different ovarian stimulation schemes on oocyte quality, the influence of auxiliary drugs added in the process of ovarian hyperstimulation on oocyte and embryo quality, the influence of clinical strategy management on clinical outcome, the new methods of evaluation of gamete and embryo quality, and current situation of basic and clinical researches and treatment strategies of ART.

【Key words】 Gamete ; Embryo ; Quality management ; Clinical outcome

高孕激素状态下促排卵方案在反复常规超促排卵失败的体外受精/卵胞质内单精子注射-胚胎移植患者中的应用

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【摘要】 目的 探讨高孕激素状态下促排卵(PPOS)方案在反复常规超促排卵方案失败的体外受精/卵胞质内单精子注射-胚胎移植(IVF/ICSI-ET)患者中的应用。方法 回顾性分析 2017 年 1 月至 2018 年 12 月期间于厦门大学附属第一医院生殖中心行长方案、拮抗剂方案促排卵失败,第 3 次促排卵继续采用常规超促排卵方案或换用 PPOS 方案行 IVF/ICSI 的 76 例正常卵巢储备功能患者资料。根据促排卵方案不同分为两组:常规超促排卵方案组(A 组)($n=46$)、PPOS 方案组(B 组)($n=30$)。比较患者使用两种促排卵方案后促排卵临床情况、实验室情况及临床妊娠结局等指标。结果 A、B 两组患者的一般情况具有可比性,B 组患者正常受精率(78.3%)、可用胚胎率(69.5%)及累积妊娠率(60.0%)均高于 A 组(70.3%, $P=0.031$; 57.9%, $P=0.017$; 34.8%, $P=0.031$),差异均有统计学意义。B 组患者优质胚胎率(52.4%)略高于 A 组(48.0%),差异无统计学意义($P=0.061$)。而两组患者的促性腺激素(Gn)使用时间、Gn 使用总量、人绒毛膜促性腺激素(hCG)注射日雌二醇水平、成熟卵数(率)、卵裂率、种植率、妊娠率、流产率等组间比较差异均无统计学意义($P>0.05$)。结论 对于采用常规超促排卵方案反复失败再次行 IVF/ICSI-ET 的卵巢储备功能正常的患者,PPOS 方案可以提高患者正常受精率、可用胚胎率及累积妊娠率,可能提高优质胚胎率,改善患者临床妊娠结局。PPOS 方案为常规超促排卵方案反复失败的卵巢储备功能正常患者再次选择促排卵方案提供一种新思路。

【关键词】 高孕激素状态下促排卵; 控制性超促排卵; 卵巢储备功能; 受精,体外; 卵胞质内单精子注射; 反复失败

基金项目:福建省自然科学基金(2019J01565)

Application of progestin-primed ovarian stimulation protocol in patients with repeated *in vitro* fertilization/intracytoplasmic sperm injection-embryo transfer failure undergoing conventional ovarian stimulations

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【Abstract】 Objective To explore the application of progestin-primed ovarian stimulation protocol in patients with repeated *in vitro* fertilization/intracytoplasmic sperm injection-embryo transfer (IVF/ICSI-ET) failure undergoing conventional controlled ovarian hyperstimulation (COH). **Methods** The clinical data of 76 patients from January 2017 to December 2018 in Reproductive Center of the First Affiliated Hospital of Xiamen University with normal ovarian reserve who failed to get pregnancy with long protocol and gonadotropin-releasing hormone (GnRH) antagonist protocol, adopting long protocol or GnRH antagonist protocol again or administered with progestin-primed

ovarian stimulation (PPOS) protocol followed by frozen-thawed embryo transfer (FET), were analyzed retrospectively. They were divided into two groups: conventional COH protocol group (group A, $n=46$), PPOS group (group B, $n=30$) according to different protocols. The clinical indicators, laboratory indicators and clinical pregnancy outcomes were compared between the two groups. **Results** The general conditions of patients in groups A and B were comparable. The normal fertilization rate (78.3%), available embryo rate (69.5%) and cumulative pregnancy rate (60.0%) in group B were higher than those in group A (70.3%, $P=0.031$; 57.9%, $P=0.017$; 34.8%, $P=0.031$). The difference was statistically significant. The high-quality embryo rate (52.4%) in group B was slightly higher than that in group A (48.0%) with no statistical significance ($P=0.061$). There were no significant differences between the two groups in the total amount of gonadotropin (Gn), the duration, estradiol level on human chorionic gonadotropin (hCG) injection day, amount and rate of M_{II} oocytes, the number of two pronucleus (2PN) embryos, the cleavage rate, the implantation rate, the clinical pregnancy rate, and the early abortion rate ($P>0.05$). **Conclusion** For the patients with normal ovarian reserve function who failed to get pregnancy repeatedly with conventional COH protocols, PPOS protocol can improve the normal fertilization rate, the available embryo rate and the cumulative pregnancy rate, and may increase the high-quality embryo rate and eventually improve clinical pregnancy outcome. PPOS protocol provides a new way for these patients to choose COH protocol thirdly.

【Key words】 Progesterin-primed ovarian stimulation ; Controlled ovarian hyperstimulation ; Ovary reserve ; Fertilization *in vitro* ; Intracytoplasmic sperm injection ; Repeated failure

Fund program : Fujian Province Natural Science Foundation (2019J01565)

·配子胚胎专栏·

选择性单胚胎移植策略探讨与临床结局分析

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【摘要】 目的 探讨第3日选择性单胚胎移植(elective single embryo transfer, eSET)在临床上的应用价值。方法 回顾性分析2014年5月至2019年3月期间在天津市第一中心医院生殖医学科予常规体外受精/卵胞质内单精子显微注射(IVF/ICSI)助孕治疗且年龄 ≤ 38 岁患者的临床资料。新鲜与解冻周期分别统计，按照移植胚胎数目，分为单胚胎移植组、双胚胎移植组；按照胚胎质量，分为单优质胚胎移植组、双优质胚胎移植组及单优质胚胎搭配非优质胚胎移植组(一优一非组)；另外，解冻周期单胚胎与双胚胎移植组再细分为卵裂胚组与囊胚组，分别比较各组间患者的临床妊娠结局。结果 在新鲜周期中，单胚胎与双胚胎移植组患者的临床妊娠率与早期流产率组间差异无统计学意义($P>0.05$)，双胚胎移植组种植率(36.22%)低于单胚胎移植组(50.77%， $P=0.002$)，而多胎妊娠率(29.86%)高于单胚胎移植组(0%， $P<0.001$)；在解冻周期中，单胚胎与双胚胎移植组临床妊娠率、种植率与早期流产率差异均无统计学意义($P>0.05$)，双胚胎移植组多胎妊娠率(30.35%)高于单胚胎移植组(2.50%)，差异有统计学意义($P<0.001$)。新鲜与解冻周期单优质胚胎组、双优质胚胎组及一优一非组3组间患者的临床妊娠率、早期流产率差异均无统计学意义($P>0.05$)，新鲜周期单优质胚胎组多胎妊娠率(0%)显著低于双优质胚胎组(32.21%)及一优一非组(6.98%， $P<0.001$)，解冻周期单优质胚胎组多胎妊娠率(0%)显著低

于双优质胚胎组(33.47%)及一优一非组(16.67%, $P<0.001$)。解冻周期卵裂胚组与囊胚组单胚胎与双胚胎移植组患者临床妊娠率、种植率、早期流产率、多胎妊娠率差异均无统计学意义(P 均 >0.05)。结论 对于有 1~2 个优质胚胎,特别是多胎相关风险高的患者更适合行第 3 日移植。第 3 日 eSET 是一个能更好地降低多胎妊娠风险的移植策略,选择优质胚胎移植或冷冻,非优质胚胎继续培养如形成囊胚根据评分进行冷冻。解冻移植仍获得较好的临床妊娠率,具有较高的利用价值。

【关键词】 妊娠率; 选择性单胚胎移植; 囊胚培养; 种植率; 多胎率

Elective single embryo transfer strategy and clinical outcome analysis

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【Abstract】 **Objective** To evaluate the clinical value of elective single embryo transfer (eSET)

on day 3. **Methods** A retrospective study was conducted on patients aged ≤ 38 years who received conventional *in vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI) assisted reproduction treatment in the Department of Reproductive Medicine of Tianjin First Central Hospital from May 2014 to Mar 2019. According to the number of transferred embryos, they were divided into single embryo transfer group and double embryo transfer group; according to the embryo quality, they were divided into single high-quality embryo transfer group, double high-quality embryo transfer group and single high-quality embryo matching non-high-quality embryo transfer group (one excellent one non group); in addition, the single embryo and double embryo transfer groups were subdivided into cleavage embryo group and blastocyst group. The clinical pregnancy outcomes were compared among these groups. **Results** There was no statistically significant difference in the clinical pregnancy rate and the early abortion rate between the single embryo and double embryos transfer groups ($P>0.05$) in the fresh cycle. The implantation rate (36.22%) of the double embryo transfer group was lower than that of the single embryo transfer group (50.77%) ($P=0.002$), while the multiple pregnancy rate (29.86%) was higher than that of the single embryo transfer group (0%) ($P<0.001$). There was no significant difference in the clinical pregnancy rate, the implantation rate and the early abortion rate between the single embryo and double embryo transfer group ($P>0.05$) in thawing cycles, while the multiple pregnancy rate in the double embryo transfer group (30.35%) was higher than that of the single embryo transfer group (2.50%) ($P<0.001$). There was no statistically significant difference in the clinical pregnancy rate, the early abortion rate among single high-quality embryo group, double high-quality embryo group and a high-quality with a poor embryo transfer group ($P>0.05$) in fresh and thawing cycles. The multiple pregnancy rate of single high-quality embryo group (0%) was significantly lower than that of double high-quality embryo group and a high-quality with a poor-quality embryo transfer group in fresh cycles (32.21%, 6.98%) ($P<0.001$), and the same as in thawing cycles (33.47%, 16.67%) ($P<0.001$). There were no significant differences in the clinical pregnancy rate, the implantation rate, the early abortion rate, and multiple pregnancy rate between the cleavage embryo group and the blastocyst group (all $P>0.05$) in thawing cycles. **Conclusion** The third day transplantation is more suitable for patients with 1 or 2 high-quality embryos, especially those with a high risk of multiple fetuses. eSET on the third day is a transplantation strategy that can better reduce the risk of multiple pregnancies. High-quality embryos are selected for transplantation or freezing, while non-high-quality embryos are further cultured and frozen according to the score for blastocyst formation. Thawed transplantation still has a good clinical pregnancy rate and has a high utilization value.

【Key words】 Pregnancy rate; Elective single embryo transfer; Blastocyst culture;

Implantation rate; Multiple pregnancy rate

抗苗勒管激素水平与卵子、胚胎质量和数量的相关性及其对获卵数的预测

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【摘要】 目的 探讨抗苗勒管激素(AMH)水平是否能作为评估卵子及胚胎质量和数量的指标，并建立获卵数的诺曼(nomogram)模型。方法 回顾性分析 2017 年 1 月 1 日至 2017 年 12 月 31 日期间在昆明医科大学第二附属医院生殖医学科行辅助生殖体外受精(IVF)周期的患者资料，分析 AMH 水平与卵子、胚胎质量和数量的相关性，并依据相关性建立获卵数诺曼预测模型。结果 共纳入 1280 例患者资料。AMH 水平与获卵数、成熟卵数、胚胎数和优质胚胎数呈显著相关(P 均 <0.001)，与成熟卵率有相关性($P=0.004$)，与优质胚胎率没有相关性($P=0.706$)。根据上述因素构建获卵数的预测模型，获卵数 $=0.046\times\text{AMH}+0.006\times\text{年龄}+(-0.015)\times\text{基础卵泡刺激素(FSH)}+(-0.003)\times\text{促性腺激素(Gn)起始用量}+2.826$ 。最后用 1280 例患者数据验证诺曼模型结果显示，共 1171 例患者的预测获卵数与实际获卵数相符，符合度为 91.5%。结论 AMH 水平可以作为评估卵子或胚胎数量的指标，但其关联性需要进一步分析说明。建立的诺曼模型可以用于临床对卵巢正常反应人群获卵数的预测及 Gn 起始剂量的选择。

【关键词】 抗苗勒管激素； 卵子质量； 胚胎质量； 获卵数； 诺曼模型

Correlation of anti-Müllerian hormone level with the quality and quantity of oocytes and embryos and its prediction for oocyte retrieved

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【Abstract】 Objective To explore whether anti-Müllerian hormone (AMH) level can be used as an indicator to evaluate the quality and quantity of oocytes and embryos, and to establish a nomogram prediction model for the prediction of oocyte retrieved. **Methods** A total of 1280 *in vitro* fertilization (IVF) cases from Reproductive Medicine Center, the Second Affiliated Hospital of Kunming Medical University were retrospectively analyzed for the correlation of AMH level with the quantity and quality of oocytes and embryos. Besides, a nomogram model was established for predicting oocytes retrieved. **Results** AMH level was significantly correlated with the number of oocytes retrieved, mature oocytes, embryos and high-quality embryos (all $P<0.001$), and was relevant to the rate of mature oocytes ($P=0.004$), but had no correlation with the rate of high-quality embryos ($P=0.706$). The nomogram model was oocytes retrieved $=0.046\times\text{basal AMH}+0.006\times\text{age}+(-0.015)\times\text{basal follicle stimulating hormone (FSH)}+(-0.003)\times\text{gonadotropin (Gn) starting dose}+2.826$. Finally the 1280 cases were used to verify the nomogram model. The results showed that the predicted number of oocytes in 1171 patients was consistent with the actual number of oocytes with a coincidence of 91.5%. **Conclusion** AMH level can be used as an indicator to assess the number of oocytes or embryos, but its relevance needs further analysis. The establishment of nomogram model in this research can predict the number of oocytes retrieved and Gn starting dosage in normal ovarian response patients.

【Key words】 Anti-Müllerian hormone； Oocyte quality； Embryo quality； Oocyte retrieved； Nomogram model

卵泡微环境中外泌体对体外受精-胚胎移植妊娠结局的影响

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【摘要】 目的 研究卵泡微环境中外泌体对体外受精-胚胎移植(IVF-ET)妊娠结局的影响, 明确卵泡微环境中外泌体的来源。方法 本研究回顾性分析了2016年12月至2018年12月期间就诊于宁夏医科大学总医院生殖中心采用IVF助孕的200例卵巢功能正常的年轻不孕患者, 观察其卵泡液中外泌体的形态并检测外泌体的浓度, 采用logistic回归及多变量偏相关分析卵子质量及妊娠结局的影响因素, 通过聚合酶链式反应(PCR)明确外泌体的来源。结果 基础卵泡刺激素(FSH)($r=0.17$, $P=0.017$)及卵泡液中外泌体浓度($r=0.881$, $P<0.001$)是影响优质胚胎率的独立因素, 基础窦卵泡数(AFC)($B=0.107$, $P=0.033$)及卵泡液中外泌体的浓度($B=0.419$, $P<0.001$)是影响妊娠结局的独立因素。PCR表明两组研究对象的外泌体均表达卵子的标志物生长分化因子(GDF)9和骨形态发生蛋白(BMP)15。结论 卵泡液中外泌体浓度是影响妊娠结局的独立因素;发育后期卵泡中的外泌体可能来源于卵细胞。

【关键词】 外泌体; 卵泡微环境; 卵泡液; 妊娠结局; 受精, 体外; 胚胎移植

Effect of exosome in follicular microenvironment on pregnancy outcome of *in vitro* fertilization and embryo transfer

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【Abstract】 Objective To study the effect of exosomes in the follicular microenvironment on the *in vitro* fertilization (IVF) pregnancy outcome, and to clarify the source of exosomes in the follicular microenvironment. **Methods** A total of 200 young patients with normal ovarian function who underwent IVF therapy were recruited in this retrospective study. The patients were divided into two groups (pregnancy and non-pregnancy) according to the pregnancy outcome. The morphology of exosomes in follicular fluid was observed and the concentration of exosomes was detected. The logistic regression analysis and multivariate partial correlation were used to analyze the factors affecting oocyte quality and pregnancy outcome. The source of exosomes was identified by polymerase chain reaction (PCR). **Results** The baseline follicle stimulating hormone (FSH) level ($r=0.17$, $P=0.017$) and the concentration of exosomes in follicular fluid ($r=0.881$, $P<0.001$) were independent factors affecting the rate of high-quality embryos. Antral follicle count (AFC) ($B=0.107$, $P=0.033$) and the concentration of exosomes in follicular fluid ($B=0.419$, $P<0.001$) were independent factors affecting the pregnancy outcome. The results of PCR showed that exosomes of both groups expressed growth differentiation factor (GDF) 9 and bone morphogenetic protein (BMP) 15 gene transcripts of oocyte markers. **Conclusion** The concentration of exosomes in follicular fluid was an

independent factor affecting the rate of pregnancy outcome. The exosomes in the late development follicular fluid are derived from oocytes

【Key words】 Exosome ; Follicular microenvironment ; Follicular fluid ; Pregnancy outcome ; Fertilization *in vitro* ; Embryo transfer

·配子胚胎专栏·

人自体单个核细胞对体外胚胎和子宫内膜共培养模型中白血病抑制因子及其受体表达的影响

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【摘要】 目的 建立胚胎和子宫内膜共培养模型，探讨人自体单个核细胞(PBMCs)对培养液中白血病抑制因子(LIF)和胚胎表面 LIF 受体(LIFR)表达的影响。方法 于 2015 年 5 月至 2016 年 5 月期间，选择在郑州大学第二附属医院行辅助生殖技术助孕反复种植失败患者的内膜 12 例，分离出子宫内膜细胞。收集其外周血分离出 PBMCs。收集 2009 年至 2014 年行辅助生殖技术助孕成功且分娩的患者的废弃胚胎。研究分为实验组（内膜-胚胎-PBMCs 共培养）和对照组（内膜-胚胎共培养）。共培养系统加入含雌孕激素培养液当日为培养第 0 日。应用酶联免疫法检测培养后第 1、第 3、第 5 日两组培养液中 LIF 的浓度；应用免疫荧光方法检测实验组和对照组培养第 5、第 6 日所形成囊胚表面 LIF 受体的表达情况，用 Image J 软件分析免疫荧光图像。结果 培养第 3 日实验组和对照组培养液中 LIF 浓度差异无统计学意义($P>0.05$)，培养第 5 日时，实验组培养液中 LIF 浓度 $[(2\ 840.02\pm240.51)\text{ ng/L}]$ 明显高于对照组 $[(2\ 411.35\pm311.63)\text{ ng/L}]$ ($P=0.001$)。囊胚 LIFR 的免疫荧光吸光度(A)值实验组大于对照组($0.255\ 8\pm0.037\ 2$ 比 $0.190\ 6\pm0.040\ 4$ ， $P=0.001$)。结论 在体外子宫内膜-胚胎共培养模型中，人自体 PBMCs 能提高子宫内膜 LIF 的表达，同时促进囊胚表面 LIFR 受体的形成，在胚胎着床过程中起重要作用。

【关键词】 人外周血单个核细胞； 反复种植失败； 白血病抑制因子； 共培养

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Effects of human autologous mononuclear cells on expression of leukemia inhibitory factor and its receptor in co-culture model of embryo and endometrium *in vitro*

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【Abstract】 Objective To investigate the effects of human autologous mononuclear cells (PBMCs) on the expression of leukemia inhibitory factor (LIF) and leukemia inhibitory factor receptor

(LIFR) on embryonic surface in co-culture model of embryo and endometrium. **Methods** From May 2015 to May 2016, endometrial glandular epithelial cells were isolated from 12 patients diagnosed as repeated implantation failure in the Second Affiliated Hospital of Zhengzhou University. PBMCs cells were isolated from their peripheral blood. We collected abandoned embryos (signed informed consent of abandoned embryos) from patients who had successfully delivered by assisted reproductive technology from 2009 to 2014. The study was divided into two groups. The experimental group was endometrium-embryo-PBMCs co-culture, and control group was endometrium-embryo co-culture. The day on which the culture medium containing estrogen and progesterone was added was regarded as the 0th day of culture. The concentration of LIF was detected by enzyme linked immunosorbent assay on the 1st, 3rd and 5th day after culture. The expression of LIFR on blastocyst surface was detected by immunofluorescence on the 5th and 6th day after culture in experimental group and control group. Immunofluorescence images were analyzed by Image J software. **Results** On the 3rd day of culture, there was no significant difference in LIF concentration between experimental group and control group ($P>0.05$). On the 5th day of culture, LIF concentration in experimental group [$(2\ 840.02\pm240.51)$ ng/L] was significantly higher than that in control group [$(2\ 411.35\pm311.63)$ ng/L] ($P=0.001$). The immunofluorescence absorbance (A) value of LIFR in blastocysts of experimental group was higher than that of control group ($0.255\ 8\pm0.037\ 2$ vs. $0.190\ 6\pm0.040\ 4$, $P=0.001$). **Conclusion** Human PBMCs can enhance the expression of LIF in endometrium and promote the expression of LIFR on blastocyst surface, which plays an important role in embryo implantation.

【Key words】 Peripheral blood mononuclear cells ; Repeated implantation failure ; Human leukemia inhibitory growth factor ; Co-culture

Fund program : Science and Technology Research Project of Science and Technology Department of Henan Province (162102310207); General Key Projects of Henan Health and Family Planning Commission (201702085); Basic Research of Science and Technology Department of Henan Province (142300410240)

·配子胚胎专栏·

生长激素在体外受精助孕中的应用进展

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【摘要】 目前越来越多的不孕女性需要借助辅助生殖技术完成妊娠,然而在体外受精-胚胎移植(IVF-ET)过程中一部分患者常常由于卵巢反应性差、卵泡发育不良和子宫内膜容受性差导致妊娠成功率降低。提高患者卵巢反应性、卵母细胞质量和子宫内膜容受性以改善 IVF-ET 结局成为了广大临床及实验室工作者共同面临的挑战,这成为辅助生殖领域的一大难题。生长激素主要作用是促进全身组织器官生长,尤其是骨骼与肌肉组织,还能调节体内三大物质的代谢,促进蛋白质合成,抑制脂肪代谢,升高血糖等。研究显示生长激素在女性生殖健康中也发挥了巨大作用,主要表现在增加卵巢对促性腺激素的反应性,优化卵泡及卵子质量,提高胚胎质量,增加子宫内膜厚度从而提高子宫内膜容受性等。本篇综述就生长激素对女性生殖系统的作用、适用人群及用法展开论述。

【关键词】 生长激素； 卵巢反应性； 卵母细胞质量； 子宫内膜容受性； 适用人群； 用法

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Application of growth hormone in *in vitro* fertilization assisted pregnancy

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【Abstract】 At present, more and more infertile women need to use assisted reproductive technology to complete pregnancy. However, in the *in vitro* fertilization and embryo transfer (IVF-ET) process, some patients often have lower pregnancy success rate due to poor ovarian reactivity, poor follicular dysplasia and poor endometrial receptivity. Increased ovarian responsiveness, oocyte quality and endometrial receptivity to improve IVF-ET outcomes has become a common challenge for clinical and laboratory workers, which has become a major problem in the field of assisted reproduction. The main role of growth hormone is promoting the growth of whole body tissues and organs, especially bones and muscles. It can also regulate the metabolism of three major substances in the body, promote protein synthesis, inhibit fat metabolism, raise blood sugar, etc. At this stage, growth hormone also plays a huge role in female reproductive health, mainly in increasing the ovarian response to gonadotropins, optimizing follicle oocyte quality, improving embryo quality, increasing endometrial thickness and improving endometrial receptivity. This review focuses on the role of growth hormone in the female reproductive system, the applicable population and usage.

【Key words】 Growth hormone ; Ovarian reactivity ; Oocyte quality ; Endometrial receptivity ; Applicable population ; Usage

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·配子胚胎专栏·

改善高龄女性卵母细胞质量的抗氧化剂及其辅助用药

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【摘要】 高龄女性生育力降低的主要原因是卵巢储备减少和染色体畸变率增加，导致流产率和染色体非整倍性的风险增加。卵母细胞质量是影响辅助生殖技术结局的关键因素，线粒体是卵母细胞中最丰富的细胞器，对卵母细胞成熟、受精和胚胎发育至关重要。但根据氧化应激——线粒体突变理论，卵巢衰老的根本原因为活性氧(reactive oxygen species, ROS)大量增加，诱导线粒体DNA(mitochondrial DNA, mtDNA)在组织中的缺失和点突变的累积、细胞凋亡增加、三磷酸腺苷(ATP)合成减少及氧化剂形成增加，从而导致卵母细胞成熟停止、染色体错位和胚胎发育受损。因此，补充

抗氧化剂可以减少线粒体氧化损伤相关的病症,增加染色体分离的能量,从而改善高龄女性卵母细胞和胚胎的质量,获得更好的妊娠结局。本文将综述抗氧化剂及辅助用药改善高龄女性卵母细胞线粒体功能的研究进展。

【关键词】 卵母细胞; 抗氧化剂; 高龄女性; 辅助用药

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Study on antioxidants and auxiliary drugs for improving oocyte quality in advanced women

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【Abstract】 The main causes of reduced fertility in advanced women are decreased ovarian reserve and increased rate of chromosomal aberrations, leading to increased risk of abortion and chromosome aneuploidy. Oocyte quality is a key factor affecting the outcome of assisted reproductive technology. Mitochondria are the most abundant organelles in oocytes, which are essential for oocyte maturation, fertilization and embryonic development. However, according to the oxidative stress-mitochondrial catastrophe theory, the basic reason of ovarian aging is the increase of reactive oxygen species (ROS), which induces the loss of mitochondrial DNA (mtDNA) in tissues and the accumulation of point mutations, increased cell apoptosis and oxidant formation, and reduced adenosine triphosphate (ATP) synthesis. This leads to the oocyte fail to maturation, chromosomal misplacement and impaired embryonic development. Therefore, supplementation with antioxidants can reduce the mitochondrial oxidative damage-related conditions, increase the energy of chromosome segregation and improve the quality of oocytes and embryos in advanced women, and obtain better pregnancy outcomes. Therefore, this article will review the research progress of antioxidants and adjuvant drugs to improve mitochondrial function in oocytes of advanced women.

【Key words】 Oocyte; Antioxidants; Advanced women; Auxiliary medication

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·配子胚胎专栏·

线粒体 DNA 含量测定在早期胚胎评估中的研究进展

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【摘要】 线粒体是细胞质中含量最丰富的细胞器,为细胞内各种代谢提供能量,在卵母细胞减数分裂、受精和早期胚胎发育的过程中发挥着巨大的作用。卵母细胞线粒体 DNA 含量的高低与其后续的胚胎发育潜能密切相关。本文从无创性测定线粒体 DNA 含量角度出发,就颗粒细胞、卵裂球及滋养外胚层细胞和胚胎剩余培养基及囊胚腔液中线粒体 DNA 含量测定在胚胎评估上的研究做一综述,并探讨其在早期胚胎评估中的应用前景。

【关键词】 DNA, 线粒体; 颗粒细胞; 滋养外胚层; 胚胎剩余培养基; 囊胚腔液

Research progress of mitochondrial DNA content on early embryo assessment

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【Abstract】 Mitochondria are the most abundant organelles in cytoplasm, which provide energy for various metabolism in cells. Mitochondria play an important role in oocyte meiosis, fertilization and early embryonic development. The content of mitochondrial DNA in oocytes is closely related to the development potential of subsequent embryos. From the viewpoint of non-invasive assessment of mitochondria DNA content in this context, here, we present an objective review of current research progress of mitochondria DNA content detection on granular cells, embryo cleavage cells/trophectoderm and spent culture media/blastocoele fluid, to explore its application prospect on early embryo development.

【Key words】 DNA, Mitochondrial ; Granular cells ; Trophectoderm ; Embryo surplus medium ; Blastocoele fluid

·临床报道·

子宫动脉栓塞术联合超声引导下清宫术 治疗剖宫产后瘢痕妊娠的临床分析

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【摘要】 目的 探讨子宫动脉栓塞术联合超声引导下清宫术在治疗剖宫产瘢痕部位妊娠(CSP)中的临床疗效。方法 回顾性分析 2011 年 7 月至 2018 年 1 月期间在上海交通大学医学院附属瑞金医院妇科收治的 CSP 患者 42 例，按治疗方案不同分为研究组(22 例)和对照组(20 例)，研究组行子宫动脉栓塞术联合超声引导下清宫术；对照组直接行超声引导下清宫术。研究子宫动脉栓塞术在 CSP 治疗中的疗效。结果 研究组和对照组治疗成功率分别为 95.45%(21/22)、95.00%(19/20)，组间差异无统计学意义($P>0.05$)。研究组术中及术后出血总量 $[(59.09\pm101.95) \text{ mL}]$ 、住院时间 $[(6.86\pm1.28) \text{ d}]$ 及血 β -人绒毛膜促性腺激素(hCG)恢复时间 $[(17.54\pm3.75) \text{ d}]$ 明显少于对照组 $[(212.00\pm432.54) \text{ mL}$ 、 $(9.35\pm1.98) \text{ d}$ 、 $(21.75\pm4.50) \text{ d}]$ ，差异有统计学意义($P<0.001$ ， $P<0.001$ ， $P=0.002$)。结论 子宫动脉栓塞联合超声引导下清宫术治疗剖宫产后瘢痕妊娠是安全、有效的治疗方法。

【关键词】 剖宫产术； 瘢痕子宫； 瘢痕妊娠； 子宫动脉栓塞术

Analysis of uterine artery embolisation in combination of dilation and curettage with ultrasonic in cesarean scar pregnancy

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【Abstract】 Objective To investigate the clinical effects of uterine artery embolisation in combination of dilation and curettage (D&C) to the patients with cesarean scar pregnancy (CSP).

Methods Data about the treatment of trichosanthin injection to 42 patients with CSP during the

period of July 2011 to January 2018 from Ruijin Hospital of Shanghai Jiao Tong University School of Medicine were collected and retrospective analysis of their clinical treatment was made. All the patients were divided into two groups. Women in the research group ($n=22$) underwent uterine artery embolisation in combination of dilation and curettage with ultrasonic. Women in the control group ($n=20$) underwent dilation and curettage with ultrasonic. The effect of uterine artery embolization in the treatment of CSP was studied. **Results** There was no difference in success rate between the research group [95.45% (21/22)] and control group [95.00% (19/20)] ($P>0.05$). The volume of blood loss during operation [(59.09±101.95) mL], the duration of hospital stay [(6.86±1.28) d] and time for β human chorionic gonadotropin (hCG) recovery [(17.54±3.75) d] in the research group were significantly smaller than those in the control group [(212.00±432.54) mL, (9.35±1.98) d, (21.75±4.50) d] ($P<0.001$, $P<0.001$, $P=0.002$ 1). **Conclusion** It is proved that treatment for uterine artery embolisation in combination of control with ultrasonic to the patients with CSP is safe and effective.

【Key words】 Cesarean section ; Scarred uterus ; Cesarean scar pregnancy ; Uterine artery embolisation

·现场调查·

社区绝经人群性生活现状与绝经泌尿生殖综合征的相关性研究

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【摘要】 目的 调查绝经后妇女性生活现状并分析绝经泌尿生殖综合征(GSM)等因素对其影响。方法 在2018年1月至6月期间采用问卷方式调查上海地区田林街道社区居住时长超过1年的绝经后妇女基本人口学特征及性生活现状，并通过症状及体征评估GSM，采用SPSS22.0软件进行统计分析。结果 共纳入1576例研究对象，年龄为(60.44±4.72)岁。性欲降低的患病率为57.6%，过去3个月性欲评分为1分占69.3%，过去3个月完全没有性生活占69.6%；GSM患病率为78.5%，与非GSM妇女相比，性欲降低的概率在患有GSM妇女中显著增高($P=0.002$)，性生活频率明显降低($P=0.005$)。多因素分析显示，年龄($P=0.002$ ； $OR=1.110$)、生产次数 ≥ 2 次($P=0.021$ ； $OR=2.161$)、患有GSM($P=0.011$ ； $OR=2.234$)是低性生活频率的危险因素；而性欲评分与性生活频率高低呈一致性($P<0.001$ ； $OR=0.195$)。结论 绝经后妇女性欲及性生活频率普遍较低，年龄、生产次数及GSM是导致性生活频率降低的危险因素。社会应重视这一群体的性教育，医护人员应关注其泌尿生殖道症状并及时给予科学地指导，改善绝经后妇女健康状况以提高其生活质量。

【关键词】 绝经；性生活；绝经泌尿生殖综合征；横断面；影响因素

Correlation between status of sexual life and menopausal genitourinary syndrome in community-dwelling menopausal women

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【Abstract】 Objective To investigate the status of sexual life in postmenopausal women and analyze the effects of factors such as menopausal urogenital syndrome. **Methods** Basic demographic characteristics and sexual life status of postmenopausal women resided in Tianlin Street community in Shanghai were collected by questionnaire survey from January to June 2018, and the menopausal urogenital syndrome was assessed by symptoms and signs. Statistical analysis was performed using SPSS22.0 software. **Results** A total of 1576 subjects were included, the age was (60.44±4.72) years old. The perception of decreased sexuality was 57.6%, sexuality score was 1 over the past 3 months accounted for 69.3%, no sex life over the past 3 months accounted for 69.6%. The prevalence of genitourinary syndrome (GSM) was 78.5%. With respect to the women who do not have GSM, the probability of decreased sexuality was significantly higher in women who have GSM ($P=0.002$), and the frequency of sexual life was significantly lower ($P=0.005$). Multivariate analysis showed that age ($P=0.002$; $OR=1.110$), number of parturitions ≥ 2 ($P=0.021$; $OR=2.161$), suffering from GSM ($P=0.011$; $OR=2.234$) were risk factors of lower frequency of sexual life. The sexuality score was consistent with the frequency of sexual life ($P<0.001$; $OR=0.195$). **Conclusion** The sexual desire and frequency of sexual life in postmenopausal women is generally lower. Age, number of parturitions, GSM were risk factors of lower frequency of sexual life. Society should pay attention to educating this group about sexuality, doctors should pay attention to their genitourinary symptoms and provide scientific guidance timely, to improve the sexual health status of postmenopausal women and improve their quality of life.

【Key words】 Menopause ; Sexual life ; Menopausal urogenital syndrome ; Cross-section ; Influencing factors

·个案报道·

妊娠合并嗜酸性粒细胞性胃肠炎伴腹水 1 例

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【摘要】 目的 报道 1 例以胃肠道组织中嗜酸性粒细胞的异常浸润为特征的罕见妊娠合并胃肠道疾病。**方法** 对 1 例胚胎植入前遗传学诊断后妊娠 20 周合并腹水，伴有外周血及腹水嗜酸性粒细胞异常增高的病例进行报道，并进行文献复习。**结果** 该例患者经给予糖皮质激素治疗后很快治愈，且胎儿预后良好。**结论** 糖皮质激素是治疗妊娠合并嗜酸性粒细胞性胃肠炎的有效方法。

【关键词】 嗜酸性粒细胞性胃肠炎； 胚胎植入前遗传学诊断； 妊娠； 腹水

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Pregnancy complicated with eosinophilic gastroenteritis with ascites: a case report

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【Abstract】 Objective To report an extremely rare gastrointestinal disease which is characterized by abnormal infiltration of eosinophils in gastrointestinal tissues of a pregnancy woman. **Methods** We reported a case of pregnancy complicated with eosinophilic gastroenteritis with ascites at 20 weeks of gestation after preimplantation genetic diagnosis who had abnormal increase of eosinophils both in peripheral blood and ascites, and we also reviewed relative literatures. **Results** This patient was quickly cured after glucocorticoid treatment and the fetus also had a good prognosis. **Conclusion** Glucocorticoid is an effective method to treat pregnancy with eosinophilic gastroenteritis.

【Key words】 Eosinophilic gastroenteritis ; Preimplantation genetic diagnosis ; Pregnancy ; Ascites

Fund program : National Natural Science Foundation of China (81601240, 81873817)

·综述·

剩余冻存胚胎现状问题及其处置建议

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【摘要】 近年来, 辅助生殖技术(ART)临床应用越来越广泛。体外受精-胚胎移植(IVF-ET)周期数增长、获卵方案完善及实验室技术提高, 均使助孕过程中产生了大量剩余胚胎。其中多数剩余胚胎长期不用, 冻存在生殖中心造成资源浪费, 且其管理与处置面临着一系列法律及伦理挑战。本文就剩余冻存胚胎现状问题做一总结, 并结合我中心临床经验对其处置提出几点建议, 旨在为国家有关部门制定相关政策法规提供参考。

【关键词】 剩余胚胎; 胚胎冷冻; 胚胎处置; 伦理法律

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Current status and disposition suggestions of surplus cryopreservation embryos

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【Abstract】 In recent years, assisted reproductive technology (ART) has been widely used in clinical practice. With the growth of *in vitro* fertilization and embryo transfer (IVF-ET) cycle numbers, the improvement of controlled ovarian stimulation scheme and laboratory technology, resulted in a large number of surplus embryos during the ART treatment. Many of these embryos are cryopreserved for a long time by the reproductive center, causing a waste of medical resources. The management and disposition of surplus frozen embryos face a series of legal and ethical challenges. This study summarizes the current situation of surplus cryopreservation embryos, and puts forward suggestions on the disposal of these embryos based on the clinical experience of our center, so as to provide references for relevant government departments to formulate policies and regulations.

【Key words】 Surplus embryo ; Embryo cryopreservation ; Embryo disposition ; Ethics laws

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剖宫产瘢痕妊娠的流行病学与临床诊治

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【摘要】 剖宫产瘢痕妊娠是指妊娠囊于子宫瘢痕处种植的特殊妊娠类型, 现有流行病学数据表明其发病率较低, 但常合并胎盘植入、子宫破裂、失血性休克等严重并发症。对疾病的诊断与处理大多数医生缺乏经验和循证医学证据。目前彩色多普勒超声检查和磁共振成像检查是在疾病早期诊断的主要手段, 根据不同分型应提供个体化诊疗方案。了解疾病的发病情况, 掌握相关诊断与治疗方法及其适应证, 方能最大限度减少患者治疗风险, 获得良好预后并保存生育力。同时提倡努力避免无指征剖宫产、降低剖宫产率, 减少剖宫产瘢痕妊娠的发生。

【关键词】 剖宫产瘢痕妊娠; 流行病学; 彩色多普勒超声; 期待治疗

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New thoughts about cesarean scar pregnancy: epidemiology, diagnosis and treatment

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【Abstract】 Cesarean scar pregnancy (CSP) refers to a gestational sac implanting at the site of a previous hysterotomy scar. Though the very few epidemiological studies showed a low incidence, it may lead to life threatening complications like placenta accrete, uterine rupture and hemorrhagic shock. Many doctors lack experience and evidence about the diagnosis and management. Color doppler ultrasonography and magnetic resonance imaging are major tools to make a diagnose in the early stage. Individualized treatment should be managed depending on the different type. Understand the epidemiology of the disease, master the different indications of relevant diagnosis and treatment methods, can make we minimize the patient's risk, achieve a favorable prognosis and preserve fertility. Special efforts are supposed to make on avoiding unindicated cesarean section (CS) delivery and lowering down the rate of CS to reduce the occurrence of CSP.

【Key words】 Cesarean scar pregnancy; Epidemiology; Color Doppler ultrasonography; Expectant management

Fund program: National Key Research and Development Project (2018YFC1002100)

人胎盘间充质干细胞修复卵巢早衰小鼠卵巢功能的作用和分子机制研究进展

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【摘要】 近年来, 人们对间充质干细胞(mesenchymal stem cells, MSCs)修复损伤组织的研究给予了更多关注, 也越来越多地考虑用各种不同来源的 MSCs 治疗卵巢早衰(premature ovarian failure, POF)/早发性卵巢功能不全(premature ovarian insufficiency, POI)。人胎盘间充质干细胞(hPMSCs)具有多向分化和保护内皮细胞免受损伤的能力, 是用于组织修复的种子细胞。相关研究表明 hPMSCs 移植对动物 POF 的治疗有一定的积极作用, 但 hPMSCs 并未广泛应用于临床治疗, 临床试验仍在进行中。本文讨论了 hPMSCs 治疗 POF 的可能机制, 涉及抗炎和免疫调节、促进卵泡发育和血管生成、抗颗粒细胞凋亡、氧化应激, 可为进一步研究和临床治疗提供理论依据。

【关键词】 间充质干细胞; 胎盘; 自身免疫; 早发性卵巢功能不全; 卵巢早衰

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Role and molecular mechanisms of human placenta-derived mesenchymal stem cells in the restoration of ovary function in premature ovarian failure mice

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【Abstract】 In recent years, more attention has been paid to the contributions of mesenchymal stem cells (MSCs) to tissue repair. Various MSCs are increasingly considered for the treatment of premature ovarian failure (POF)/premature ovarian insufficiency (POI). Human placenta-derived mesenchymal stem cells (hPMSCs) have become seed cells for tissue repair due to their multilineage differentiation potential and ability of protecting endothelial cells from damage. Related researches have demonstrated that hPMSCs transplantation has a certain positive effect on the treatment of POF animal, but hPMSCs are not widely used in clinical treatment, clinical trials are still in progress. We reviewed the possible mechanisms by which hPMSCs ameliorate POF, anti-inflammatory effects and immunoregulatory effects, folliculogenesis, angiogenesis, antiapoptotic effects, and oxidative stress effects, providing a theoretical basis for further research and clinical treatment.

【Key words】 Mesenchymal stem cells; Placenta; Autoimmune; Premature ovarian failure; Premature ovarian insufficiency

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2018 美国妇产科医师学会委员会意见： 青少年痛经和子宫内膜异位症 (No. 760) 的解读

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【摘要】 痛经是青少年和年轻女性最常见的经期症状，大多数青少年为原发性痛经。病史提示为原发性痛经，可直接采用非甾体抗炎药或激素治疗，效果佳。若经治疗症状仍无改善，应检查可能存在的继发性原因和治疗的依从性。子宫内膜异位症是青少年继发性痛经的首要原因，是一种慢性疾病，在青少年中常被忽视导致延误诊治，不及时治疗会进一步恶化，治疗目标是缓解症状，预防疾病进展，保护生育能力。治疗需个体化，宣教和支持也非常重要。2018 年美国妇产科医师学会(ACOG)发布了“青少年痛经和子宫内膜异位症委员会意见”，现对其进行解读。

【关键词】 痛经； 子宫内膜异位症； 青少年

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Interpretation to the American College of Obstetricians and Gynecologists' Committee Opinion No. 760: dysmenorrhea and endometriosis in the adolescent

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【Abstract】 Dysmenorrhea is the most common menstrual symptom among adolescent girls and young women. Most adolescents experiencing dysmenorrhea have primary dysmenorrhea. When the patient's history suggests primary dysmenorrhea and will respond well to empiric treatment with nonsteroidal anti-inflammatory drugs (NSAIDs) or hormonal suppression, or both. When a patient does not experience clinical improvement for her dysmenorrhea with therapy, secondary causes and treatment adherence should be investigated. Endometriosis is the leading cause of secondary dysmenorrhea in adolescents. Endometriosis in adolescents is considered a chronic disease with potential for progression if left untreated. Adolescents are particularly susceptible to delay in accessing diagnosis and treatment. The goals of therapy include symptom relief, suppression of disease progression, and protection of future fertility. Therapy must be individualized, and long-term patient and familial education and support are also important. This paper interpreted the American College of Obstetricians and Gynecologists' Committee Opinion: dysmenorrhea and endometriosis in the adolescent.

【Key words】 Dysmenorrhea； Endometriosis； Adolescent

Fund program： Beijing Municipal Administration of Hospitals Incubating Program (PX2019053); Beijing Administration of Traditional Chinese Medicine (JJ2018-73)