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子宫腺肌病伴不孕症诊疗中国专家 共识

子宫腺肌病伴不孕症诊疗中国专家共识编写组

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【摘要】 子宫腺肌病是育龄妇女常见的妇科疾病, 子宫腺肌病合并不孕症时的诊疗方案选择是临床棘手问题, 缺乏共识性意见。为更好地规范子宫腺肌病伴不孕症的诊断和治疗, 中国妇幼保健协会生育保健专业委员会生殖外科学组专家结合国内外文献证据与临床实践, 从子宫腺肌病的临床表现、诊断、子宫腺肌病引起不孕的发病机制、子宫腺肌病伴不孕症治疗方案和路径选择等方面制定本共识, 以期指导临床实践, 改善该类患者的生育结局。

【关键词】 子宫腺肌病; 不孕症; 诊断; 治疗

指南注册: 国际实践指南注册平台 (IPGRP-2019CN087)

Chinese experts consensus on diagnosis and clinical management of adenomyosis with infertility

*Chinese Diagnosis and Clinical Management of Adenomyosis with Infertility Consensus
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【Abstract】 Adenomyosis is a common gynecological disease in women of childbearing age, and more and more attention has been paid to its relationship with infertility. In order to standardize the diagnosis and treatment of adenomyosis with infertility, experts from the Reproductive Surgery Group of the Reproductive Health Committee of Chinese Maternal and Child Health Association developed this consensus including the clinical manifestations and diagnosis of adenomyosis, the pathogenesis and treatment of infertility caused by adenomyosis according to much published evidence. The purpose of this consensus is to guide clinical practice and improve the reproductive outcome of adenomyosis patients with infertility.

【Key words】 Adenomyosis; Infertility; Diagnosis; Treatment

Guide Registration: International Practice Guideline Registry Platform (IPGRP-2019CN087)

·专家建议·

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关于准备妊娠和辅助生殖技术助孕人群新型冠状病毒疫苗接种的专家建议

北京市人类辅助生殖技术质量控制和改进中心专家组

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【摘要】 新型冠状病毒疫情暴发以来, 世界各国加快新型冠状病毒疫苗(简称新冠疫苗)的研发。已有多个候选疫苗进入Ⅲ期临床试验或附条件上市及紧急使用。

虽然所有年龄段人群均对新型冠状病毒易感, 但孕妇仍被排除在新冠疫苗Ⅲ期临床试验之外, 因此无法确定新冠疫苗对妊娠期妇女及其子代的安全性, 也缺乏孕期

及准备妊娠人群新冠疫苗有效性和安全性的数据。本专家建议参考国内外最新研究进展、相关机构推荐和我国相关政策规范，经过北京市人类辅助生殖技术质量控制和改进中心专家组讨论，为我国准备妊娠和接受辅助生殖技术助孕人群新冠疫苗接种提供指导性意见。

【关键词】 生殖技术，辅助； 新型冠状病毒； 新型冠状病毒疾病； 新型冠状病毒疫苗

基金项目： 国家自然科学基金（72042013）； 国家重点研发计划（2018YFC1002106）

COVID-19 vaccination strategy for planning pregnancy and assisted reproductive technology treatment: expert recommendations

Expert Group for Beijing Human Assisted Reproductive Technology Center For Quality Control and Improvement

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【Abstract】 The pandemic of COVID-19 has accelerated the development and production of the new coronavirus vaccine worldwide. At present, a number of candidate vaccines have been conditional marketing for emergency use and massive vaccination programs are now being undertaken. Although people of all ages are susceptible to novel coronavirus, pregnant women have traditionally been excluded from clinical trials of COVID-19 vaccines, limited data are available on their efficacy and safety during pregnancy and there is lack of data on the effectiveness and safety of COVID-19 vaccines for planning pregnancy couples. This statement reviews and summarizes relevant research and guidelines about COVID-19 vaccination, which has been discussed by the expert group of Beijing Human Assisted Reproductive Technology Center For Quality Control and Improvement, to provide recommendations on COVID-19 vaccination for planning pregnancy couples and those receiving fertility treatment.

【Key words】 Reproductive technology, assisted; 2019-novel coronavirus; Corona virus disease 2019; COVID-19 vaccination

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·临床研究·

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波塞冬分类指标对预期低预后人群 促排卵体外受精/卵胞质内单精子 注射早期治疗结局的预测价值研究

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【摘要】 目的 探索年龄、抗苗勒管激素(anti-Müllerian hormone, AMH)和窦卵泡计数(antral follicle count, AFC)对符合波塞冬分类标准“预期低预后人群”的促排卵体外受精/卵胞质内单精子注射(*in vitro* fertilization/intracytoplasmic sperm injection, IVF/ICSI)早期治疗结局的预测价值。方法 本研究回顾性分析2017年3月1日至2018年12月31日期间就诊于北京大学第三医院妇产科生殖医学中心，满足波塞冬标准预期低预后患者的IVF/ICSI周期资料。按年龄、AMH及AFC分为A组(年龄<35岁、AFC<5且AMH<1.2 μg/L)、B组(年龄≥35岁、AFC<5且AMH<1.2 μg/L)、C组(AFC<5且AMH≥1.2 μg/L)、D组(年龄<35岁、AFC≥5且AMH<1.2 μg/L)和E组(年龄≥35岁、AFC≥5且AMH<1.2 μg/L)，比较各组一般资料、促排卵结局及妊娠结局。结果 共计纳入6745个满足波塞冬标准预期低预后患者的IVF/ICSI周期。A、B组患者选用微刺激方案及自然周期取卵比例[A组15.8%(158/1000)、6.4%(64/1000)；B组28.1%(659/2342)、17.7%(414/2342)]显著高于C、D、E组[C组6.4%(54/845)、1.1%(9/845)；D组5.8%(63/1077)、0.8%(9/1077)；E组11.0%(163/1481)、0.9%(14/1481)， $P<0.001$]。A、B组患者获卵数[4(2, 6)枚，3(2, 5)枚]显著低于D、E组[7(4, 10)枚，6(3, 8)枚] (P 均<0.001)。新鲜移植周期中，年轻患者(A组、D组)的临床妊娠率[39.2%(200/510)、37.2%(272/731)]、着床率[28.4%(251/883)、26.7%(355/1332)]、活产率[24.9%(127/510)、22.3%(163/731)]显著高于高龄患者[B组：21.5%(238/1109)、14.9%(266/1787)、10.4%(115/1109)；E组：23.5%(212/903)、15.4%(243/1581)、11.8%(107/903)] (P 均<0.001)。A、B组患者移植周期取消率[49.0%(490/1000)、52.6%(1233/2342)]显著高于其他三组[C组34.1%(288/845)、D组32.1%(346/1077)、E组39.0%(578/1481)， $P<0.001$]，且因为无可移植胚胎、未获卵而取消移植周期的比例达3/4。结论 波塞冬标准对于预期低预后的人群，有较好的预测作用。AMH作为一个客观指标，对于临床妊娠率有较好的预测价值，

而 AFC 较多的患者, 预示较高的获卵数。低卵巢储备的年轻患者(即波塞冬 3 组), 移植周期临床妊娠率尚可, 但因未获卵、无可移植胚胎取消周期比例较高, 每取卵周期活产率仍较低。

【关键词】 受精, 体外; 卵巢储备; 排卵诱导; 卵巢, 低反应; 标准, 波塞冬

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Predictive value of POSEIDON classification index for the early outcome of *in vitro* fertilization/intracytoplasmic sperm injection in the expected low prognosis population

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【Abstract】 **Objective** To explore the predictive value of age, anti-Müllerian hormone (AMH) and antral follicle count (AFC) for the outcome of *in vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI) in the expected low prognosis population according to the POSEIDON criteria. **Methods** This retrospective study was performed in patients who underwent IVF/ICSI and were expected low prognosis of ovarian stimulation from March 1, 2017 to December 31, 2018 in Reproductive Medicine Center, Department of Obstetrics and Gynecology, Peking University Third Hospital. According to three of the POSEIDON classification index, cycles were divided into 5 groups: group A (age<35 years, AFC<5 and AMH<1.2 µg/L), group B (age≥35 years, AFC<5 and AMH<1.2 µg/L), group C (AFC<5 and AMH≥1.2 µg/L), group D (age<35 years, AFC≥5 and AMH<1.2 µg/L) and group E (age≥35 years, AFC≥5 and AMH<1.2 µg/L). The ovarian stimulation and pregnancy outcomes were analyzed. **Results** A total of 6745 IVF/ICSI cycles were included. The proportions of mini-stimulation and natural cycles in group A [15.8% (158/1000), 6.4% (64/1000)] and group B [28.1% (659/2342), 17.7% (414/2342)] were significantly higher than those in groups C, D and E [group C 6.4% (54/845), 1.1% (9/845); group D 5.8% (63/1077), 0.8% (9/1077); group E 11.0% (163/1481), 0.9% (14/1481), $P<0.001$]. The number of retrieved oocytes in groups A and B [4(2,6), 3(2,5)] was significantly lower than that in groups D and E [7(4,10), 6(3,8)] ($P<0.001$). The clinical pregnancy rate [39.2% (200/510), 37.2% (272/731)], the implantation rate [28.4% (251/883), 26.7% (355/1332)], and the live birth rate [24.9% (127/510), 22.3% (163/731)] of young patients in groups A and D were significantly higher than those of older patients [group B: 21.5% (238/1109), 14.9% (266/1787), 10.4% (115/1109), group E: 23.5% (212/903), 15.4% (243/1581), 11.8% (107/903)] ($P<0.001$). The cancellation rate of transplantation in groups A and B [49.0% (490/1000), 52.6% (1233/2342)] was significantly higher than that

in the other groups [group C 34.1% (288/845), group D 32.1% (346/1077), group E 39.0% (578/1481), $P<0.001$], and among the cancellation reasons, the proportion of no embryos or no retrieved eggs in groups A and B was also higher. **Conclusion** The POSEIDON criteria has a good predictive value on expected low prognosis patients. AMH, which is an objective index, represents a higher clinical pregnancy rate, while higher AFC indicate more retrieved eggs. In young patients with low ovarian reserve (POSEIDON group 3), clinical pregnancy rate per cycle is moderate, but due to a high cancellation rate because of no embryos or no retrieved eggs, live birth rate per egg retrieval cycle is still low.

【Key words】 Fertilization *in vitro*; Ovarian reserve; Ovulation induction; Ovary, poor response; Standards, POSEIDON

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早卵泡期长效方案最佳获卵数的探讨

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【摘要】 目的 探讨早卵泡期长效方案的最佳获卵数及在达到较高累积活产率 (cumulative live birth rate, CLBR) 的同时, 减少卵巢过度刺激综合征 (ovarian hyperstimulation syndrome, OHSS) 的风险。方法 回顾性队列研究分析 2014 年 1 月至 2017 年 12 月期间在郑州大学第三附属医院生殖医学科首次行体外受精或卵胞质内单精子注射助孕且采用早卵泡期长效方案的患者作为研究对象。根据获卵数进行分组, A 组: 获卵数 1~5 枚; B 组: 获卵数 6~10 枚; C 组: 获卵数 11~15 枚; D 组: 获卵数 16~20 枚; E 组: 获卵数 >20 枚, 分析 5 组患者的基础资料及临床数据。主要观察指标为 CLBR 和 OHSS 发生率。采用二元逻辑回归校正混杂因素, 分析影响 CLBR 和 OHSS 发生率的因素。结果 女方年龄的增加 ($aOR=0.93$, 95% $CI=0.90\sim0.97$, $P<0.001$) 和体质量指数的增加

($aOR=0.95$, 95% $CI=0.92\sim0.99$, $P=0.02$) 是 CLBR 的危险因素, 获卵数的增加 ($aOR=1.27$, 95% $CI=1.20\sim1.35$, $P<0.001$) 是 CLBR 的保护因素。女方年龄越小 ($aOR=0.94$, 95% $CI=0.91\sim0.97$, $P<0.001$)、体质量指数减低 ($aOR=0.96$, 95% $CI=0.93\sim0.99$, $P=0.04$)、获卵数增加 ($aOR=1.84$, 95% $CI=1.64\sim2.06$, $P<0.001$) 是 OHSS 发生率的危险因素。随着获卵数的增加 (A 组到 C 组), CLBR 增长显著, 差异有统计学意义 [51.6% (157/304)、64.8% (869/1314)、75.2% (1334/1774), $P<0.001$], 而 C 组、D 组和 E 组间 CLBR 的差异无统计学意义 ($P>0.05$)。随着获卵数增加 (A 组到 E 组), OHSS 发生率增加显著, 差异有统计学意义 [0.3% (1/304)、3.3% (44/1314)、5.0% (88/1774)、9.8% (104/1065)、15.4% (77/499), $P<0.001$], 尤其是在获卵数 >15 枚时, OHSS 发生率明显增加。结论 早卵泡期长效方案中, 获卵数在 11~15 枚, 可获得较高的 CLBR, 且 OHSS 发生率较低, 为适宜的获卵数区间。

【关键词】 获卵数; 累积活产率; 卵巢过度刺激综合征

Investigate the optimal number of oocytes retrieved of early follicular phase prolonged protocol

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【Abstract】 **Objective** To investigate the optimal number of oocytes retrieved of early follicular phase prolonged protocol and to reduce the risk of ovarian hyperstimulation syndrome (OHSS) while achieving a high cumulative live birth rate (CLBR). **Methods** It was a retrospective cohort study. Patients who underwent the first *in vitro* fertilization or intracytoplasmic sperm injection in the Reproductive Center of the Third Affiliated Hospital of Zhengzhou University from January 2014 to December 2017 were included. According to the number of oocytes retrieved, we divided all patients into 5 groups, group A: 1–5 oocytes, group B: 6–10 oocytes, group C: 11–15 oocytes, group D: 15–20 oocytes, group E: >20 oocytes. The basic and clinical data of 5 groups were analyzed. The main outcome measures were CLBR and the incidence of OHSS. Binary logistic regression was used to correct confounding factors to analyze the factors affecting the CLBR and the incidence of OHSS. We calculated the CLBR and the incidence of OHSS in each group. **Results** The maternal age ($aOR=0.93$, 95% $CI=0.90\sim0.97$, $P<0.001$) and body mass index ($aOR=0.95$, 95% $CI=0.92\sim0.99$, $P=0.02$) were risk factors for CLBR. The number of oocytes retrieved was the protection factor for CLBR ($aOR=1.27$, 95% $CI=1.20\sim1.35$, $P<0.001$). The maternal age ($aOR=0.94$, 95% $CI=0.91\sim0.97$, $P<0.001$), body mass index ($aOR=0.96$, 95% $CI=0.93\sim0.99$, $P=0.04$), and increase in the number of oocytes retrieved ($aOR=1.84$, 95% $CI=1.64\sim2.06$, $P<0.001$) were the independent risk factors of the incidence of OHSS. With the increase of the number of oocytes retrieved (group A to group C), CLBR increased significantly [51.6% (157/304), 64.8% (869/1314), 75.2% (1334/1774), $P<0.001$], while the differences among groups C, D and E were

not statistically significant ($P>0.05$). With the increase in the number of oocytes retrieved (group A to group E), the incidence of OHSS increased significantly [0.3% (1/304), 3.3% (44/1314), 5.0% (88/1774), 9.8% (104/1065), 15.4% (77/499), $P<0.001$], especially when the number of oocytes retrieved was >15 . **Conclusion** For the early follicular phase prolonged protocol, the optimal number of oocytes retrieved is 11–15, which can obtain higher CLBR, and reduce the incidence of OHSS.

【Key words】 Number of oocytes retrieved; Cumulative live birth rate; Ovarian hyperstimulation syndrome

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第 3 日移植冷冻后剩余非优质胚胎 囊胚培养的临床应用价值

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【摘要】 目的 探讨第 3 日(day 3, D3)移植冷冻后剩余非优质胚胎囊胚培养的临床应用价值, 寻找最佳的胚胎移植策略。方法 本研究回顾性队列研究分析了 2015 年 7 月至 2020 年 3 月期间在天津市第一中心医院生殖医学科行囊胚解冻移植治疗 362 个周期患者的临床资料。按照培养时间分为第 5 日(day 5, D5)囊胚移植组、第 6 日(day 6, D6)囊胚移植组, 按照移植胚胎数目分为单囊胚移植组、双囊胚移植组; 按照胚胎质量单囊胚移植组分为单优质胚胎组、单非优质胚胎组; 双囊胚移植组分为双优质囊胚组、单优搭配非优囊胚移植组(一优一非组)及双非优质胚胎组。比较各组临床妊娠率、种植率、多胎妊娠率等指标。结果 解冻周期 D5 囊胚移植组临床妊娠率、种植率均高于 D6 囊胚移植组 [62.96% (102/162)比 42.50% (85/200)、53.98% (122/226)比 35.86% (104/290)], 差异均有统计学意义 (P 均 <0.001), 早期流产率、多胎妊娠率差异均无统计学意义 (P 均 >0.05)。D5 单囊胚移植组与双囊胚移植组的临床妊娠率、早期流产率差异均无统计学意义 (P 均 >0.05), 单囊胚移植组种植率高于双囊胚移植组 [62.24%

(61/98) 比 47.66% (61/128)] , 多胎妊娠率低于双囊胚组 [3.28% (2/61) 比 46.34% (19/41)] , 差异均有统计学意义 ($P=0.029$ 、 $P<0.001$) ; D6 单囊胚移植组与双囊胚移植组临床妊娠率、多胎妊娠率 [35.45% (39/110) 比 51.11% (46/90)、5.13% (2/39) 比 26.09% (12/46)] 差异均有统计学意义 ($P=0.026$ 、 $P=0.009$) , 种植率、早期流产率差异均无统计学意义 (P 均 >0.05) 。D5、D6 单囊胚移植组单优质胚胎与非优质胚胎的临床妊娠率、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) 。D5 双囊胚移植组中双优质胚胎、一优一非、双非优质胚胎相比临床妊娠率、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) 。D6 双非优质胚胎组种植率 [26.67% (24/90)] 低于双优质胚胎组 [47.62% (20/42)] 及一优一非组 [43.75% (7/16)] , 差异有统计学意义 ($P=0.029$) , 临床妊娠率、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 D3 优质胚胎移植冷冻后, 剩余非优质胚胎继续培养形成囊胚冷冻, 解冻移植可获得较好的临床妊娠率, 提高了胚胎的利用价值, 降低患者的治疗成本。D5 囊胚质量优于 D6 囊胚, 优先选择 D5 的单囊胚移植, 在不影响临床妊娠率的情况下降低多胎妊娠率。

【关键词】 囊胚培养; 囊胚移植; 妊娠率; 冻融周期

Clinical application value of blastocysts derived from poor-quality embryos after day 3 transplantation and frozen

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【Abstract】 **Objective** To evaluate the clinical value of blastocysts derived from poor-quality embryos after day 3 (D3) transplantation and frozen, to investigate the best embryo strategies of frozen-thawed blastocysts. **Methods** A retrospective cohort study was conducted on 362 frozen-thawed blastocyst transfer cycles were retrospectively analyzed in the Department of Reproductive Medicine, Tianjin First Central Hospital from July 2015 to March 2020. According to the days of culture, they were divided into day 5 (D5) and day 6 (D6) blastocyst transplantation group; according to the number of embryos transferred, they were divided into single blastocyst transplantation group and double blastocyst transplantation group; according to the embryo quality, single blastocyst transplantation group was divided into single high-quality embryo group and single poor-quality embryo group. The double blastocyst transplantation group was divided into double high-quality blastocyst group, a high-quality embryo matching a poor-quality blastocyst transplantation group and the double poor-quality blastocyst group. Clinical pregnancy rate, implantation rate and multiple pregnancy rate were compared in each group. **Results** The clinical pregnancy rate and the implantation rate of D5 blastocyst transplantation group in thawing cycles were higher than those of D6 blastocyst transplantation group [62.96% (102/162) vs. 42.50% (85/200), 53.98% (122/226) vs. 35.86% (104/290)] (all $P<0.001$), and there was no statistically significant difference of early abortion rate and multiple

pregnancy rate between the D5 and D6 groups ($P>0.05$). There was no statistically significant difference in the clinical pregnancy rate and the early abortion rate of D5 single blastocyst groups and double blastocyst pregnancy ($P>0.05$), the implantation rate of single blastocyst group was higher than that of the double blastocyst group [62.24% (61/98) vs. 47.66% (61/128)] while the multiple pregnancy rate of single blastocyst group was lower than that of the double blastocyst group [3.28% (2/61) vs. 46.34% (19/41)] ($P=0.029$, $P<0.001$). The clinical pregnancy rate and the multiple pregnancy rate of D6 single blastocyst group were lower than those of D6 double blastocyst pregnancy group [35.45% (39/110) vs. 51.11% (46/90), 5.13% (2/39) vs. 26.09% (12/46)] ($P=0.026$, $P=0.009$), there were no statistically significant differences in implantation rate and early abortion rate (all $P>0.05$). There were no statistically significant differences in clinical pregnancy rate, implantation rate, early abortion rate and multiple pregnancy rate between single high-quality embryo and poor-quality embryo group in D5 and D6 single blastocyst transplantation group (all $P>0.05$). There were no statistically significant differences in clinical pregnancy rate, implantation rate, early abortion rate, and multiple pregnancy rate of the double high-quality blastocyst transplantation group, a high-quality embryo matching a poor-quality blastocyst transplantation group and the double poor-quality blastocyst group in D5 ($P>0.05$). The implantation rate of D6 double poor-quality embryo group [26.67% (24/90)] was lower than that of the double high-quality embryo group [47.62% (20/42)] and a high-quality embryo matching a poor-quality embryo group [43.75% (7/16)] ($P=0.029$), while there were no statistically significant differences in clinical pregnancy rate, early abortion rate, and multiple pregnancy rate (all $P>0.05$). **Conclusion** After the high-quality D3 embryo transfer and freezing, the remaining poor-quality embryos can be cultured to form blastocyst, better clinical pregnancy rate was obtained for transfer the frozen-thawed blastocysts, it increases the value of embryos and reduces the cost of treatment. The quality of D5 blastocyst is better than that of D6 blastocyst. The single blastocyst transplantation of D5 is preferred to reduce the rate of multiple pregnancy without affecting the clinical pregnancy rate.

【Key words】 Blastocyst culture; Blastocyst transfer; Pregnancy rate; Frozen-thawed cycle

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两种促性腺激素释放激素激动剂降调节方案晚卵泡期孕酮升高的临床结局分析

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【摘要】 目的 探讨卵泡期长效方案和黄体期短效方案晚卵泡期孕酮升高对临床结局的影响。方法 回顾性队列研究分析 2015 年 1 月至 2018 年 12 月期间在郑州大学第一附属医院生殖医学中心接受新鲜卵裂期胚胎移植助孕并采用卵泡期长效方案或黄体期短效方案的体外受精/卵胞质内单精子显微注射 (*in vitro* fertilization/intracytoplasmic sperm injection, IVF/ICSI) 的患者临床资料。对上述患者周期进行针对年龄、基础卵泡刺激素 (follicle-stimulating hormone, FSH) 和移植胚胎数的倾向性评分匹配 (propensity score matching, PSM), 采用卵泡期长效方案患者 (A 组) 1748 例, 采用黄体期短效方案患者 (B 组) 1751 例。根据人绒毛膜促性腺激素 (human chorionic gonadotropin, hCG) 注射日孕酮水平再分别将 A 组、B 组患者分为 4 个亚组: <1.00 $\mu\text{g/L}$ 组 (1 亚组), 1.00~1.25 $\mu\text{g/L}$ 组 (2 亚组), 1.25~1.75 $\mu\text{g/L}$ 组 (3 亚组) 和 1.75~3.00 $\mu\text{g/L}$ 组 (4 亚组)。比较 A、B 组内各亚组临床妊娠率、流产率等各项指标。结果 A 组的临床妊娠率高于 B 组 [65.5% (1145/1748) 比 53.6% (938/1751), $P<0.001$], 活产率高于 B 组 [55.7% (973/1748) 比 44.0% (770/1751), $P<0.001$], 差异均有统计学意义。A 组中 A4 亚组临床妊娠率 [56.6% (82/145)] 显著低于 A1 亚组 [66.8% (725/1086), $P=0.01$] 和 A2 亚组 [69.3% (167/241), $P=0.008$]; B 组中 B3 和 B4 亚组临床妊娠率 [43.6% (68/156), 30.8% (12/39)] 显著低于 B1 亚组 [55.4% (728/1315)] 和 B2 亚组 [55.2% (127/230)], 差异均具有统计学意义 (B3 比 B1 亚组: $P=0.003$; B4 比 B1 亚组: $P=0.002$; B3 比 B2 亚组: $P=0.016$; B4 比 B2 亚组: $P=0.004$)。调整混杂因素后, 多因素 logistics 分析结果显示, A 组中其他亚组与 A1 亚组相比, 对临床妊娠率影响差异无统计学意义 (A2 亚组比 A1 亚组, $OR=1.090$, 95% $CI=0.787\sim1.509$, $P=0.606$; A3 亚组比 A1 亚组, $OR=0.809$, 95% $CI=0.588\sim1.114$, $P=0.194$; A4 亚组比 A1 亚组, $OR=0.675$, 95% $CI=0.456\sim1.000$, $P=0.050$); B 组中与 B1 亚组相比, B4 亚组临床妊娠率明显下降 ($OR=0.410$, 95% $CI=0.199\sim0.843$, $P=0.015$)。结论 经过 PSM 匹配后, 卵泡期长效方案临床妊娠率、活产率优于黄体期短效方案。卵泡期长效方案对高孕酮负面影响的耐受性优于黄体期短效方案。

【关键词】 垂体降调节; 孕酮升高; 临床结局

Analysis of clinical pregnancy outcome of progesterone elevation with two kinds of down-regulation methods using gonadotropin-releasing hormone agonist

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【Abstract】 Objective To evaluate the clinical pregnancy outcomes of progesterone elevation cycles with follicular phase gonadotropin-releasing hormone agonist (GnRH-a) long-acting protocol and luteal phase GnRH-a short-acting protocol. **Methods** In this retrospective cohort study, data of patients who received *in vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI) treatment with fresh cleavage phase embryo transferred and follicular phase GnRH-a long-acting protocol or luteal phase GnRH-a short-acting protocol at the Reproductive Medical Center of the First Affiliated Hospital of Zhengzhou University between January 2015 and December 2018 were analyzed. We matched the above patient cycles with age, basal follicle-stimulating hormone (FSH) and number of transplanted embryos using propensity score matching (PSM). There were 1748 cases received long-acting protocol (group A) and 1751 cases received short-acting protocol (group B). According to the different concentrations of progesterone on human chorionic gonadotropin (hCG) injection day, patients were divided into four subgroups: $<1.00 \mu\text{g/L}$ (group 1), $1.00\text{--}1.25 \mu\text{g/L}$ (group 2), $1.25\text{--}1.75 \mu\text{g/L}$ (group 3) and $1.75\text{--}3.00 \mu\text{g/L}$ (group 4). We compared the different items among subgroups in group A and group B including clinical pregnancy, miscarriage rate, and so on. **Results** The clinical pregnancy rate of group A was higher than that of group B [65.5% (1145/1748) vs. 53.6% (938/1751), $P<0.001$], and the live birth rate of group A was higher than that of group B [55.7% (973/1748) vs. 44.0% (770/1751), $P<0.001$], both of the differences were statistically significant. The clinical pregnancy rate of subgroup A4 [56.6% (82/145)] was significantly lower than that of subgroup A1 [66.8% (725/1086), $P=0.010$] and subgroup A2 [69.3% (167/241), $P=0.008$]. In group B, the clinical pregnancy rate of subgroup B3 and subgroup B4 [43.6% (68/156), 30.8% (12/39)] was significantly lower than that of subgroup B1 [55.4% (728/1315)] and subgroup B2 [55.2% (127/230)], the differences were statistically significant (subgroup B3 vs. subgroup B1, $P=0.003$; subgroup B4 vs. subgroup B1, $P=0.002$; subgroup B3 vs. subgroup B2, $P=0.016$; subgroup B4 vs. subgroup B2, $P=0.004$). Adjusted for confounding factors, the results of multi-factor logistics analysis showed that: compared with subgroup A1, other subgroups (subgroup A2: $OR=1.090$, 95% $CI=0.787\text{--}1.509$, $P=0.606$; subgroup A3: $OR=0.809$, 95% $CI=0.588\text{--}1.114$, $P=0.194$; subgroup A4: $OR=0.675$, 95% $CI=0.456\text{--}1.000$, $P=0.050$) in group A had no statistically significant difference in clinical pregnancy rate. Compared with subgroup B1, the clinical pregnancy rate of subgroup B4 was significantly lower in group B ($OR=0.410$, 95% $CI=0.199\text{--}0.843$, $P=0.015$). **Conclusion** After PSM matching, the clinical pregnancy rate and the live birth rate of follicular phase GnRH-

a long-acting protocol were better than those of luteal phase GnRH-a short-acting protocol. The follicular phase GnRH-a long-acting protocol had better tolerance to the negative effects of high progesterone than that of luteal phase GnRH-a short-acting protocol.

【Key words】 Pituitary down-regulation; Progesterone elevation; Clinical pregnancy outcome

·临床研究·

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少弱精子症患者 *DAZL* 基因 DNA 甲基化分析

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【摘要】 目的 比较正常生育男性及少弱精子症患者 *DAZL* 基因启动子区域 DNA 甲基化水平的差异。方法 采用病例对照研究, 回顾性分析 2018 年 6 月至 2019 年 6 月期间于徐州医科大学附属连云港医院就诊的具有正常生育男性(对照组) 15 例和少弱精子症患者 35 例(少弱精子症组)的临床资料, 对精液标本进行精子形态与精子浓度、活力分析。提取精液基因组 DNA 行亚硫酸氢盐处理, 利用 PCR 体外扩增并将 PCR 产物经纯化后与 pCR2.1 载体连接及酶切验证, 挑选阳性克隆进行测序和 DNA 甲基化程度差异比较。结果 对照组 *DAZL* 基因启动子均呈低甲基化水平, 甲基化率为 $0.96\% \pm 0.46\%$, 少弱精子症组甲基化率为 $12.15\% \pm 11.35\%$, 组间差异有统计学意义 ($P=0.0004$); *DAZL* 基因甲基化率在少弱精子症组患者中个体差异明显, 有 12 例 (34.3%) 患者 DNA 甲基化水平超

过 10%。结论 *DAZL* 基因启动子区域甲基化异常可能和少弱精子症有关,有望成为男性生精缺陷的生物学标志之一。

【关键词】 男性不育; *DAZL* 基因; 少弱精子症; DNA 甲基化; 重亚硫酸盐测序 PCR

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Analysis of DNA methylation status of *DAZL* in semen from men with oligoasthenozoospermia

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【Abstract】 **Objective** To compare the DNA methylation levels of *DAZL* promoter regions in spermatozoa between the normozoospermic and oligoasthenozoospermic males. **Methods** A case-control study was performed. Routine semen analysis and morphological analysis were performed in 15 normozoospermic individuals (control group) and 35 subfertile patients with oligoasthenozoospermia (oligoasthenozoospermia group). Semen were purified by density gradient centrifugation. DNA was extracted, treated with bisulfite, amplified by PCR and the purified PCR products were cloned into pCR2.1 vector and then proceeded to chemical transformation, restriction enzyme reaction. The positive clones of each sample were selected for sequencing analysis and DNA methylation analysis. **Results** The DNA methylation rate of *DAZL* promoters was increased significantly in oligoasthenozoospermia group (12.15%±11.35%) compared with control group (0.96%±0.46%) ($P=0.0004$). There was also an obvious difference in the DNA methylation status among oligoasthenozoospermia males. DNA methylation levels were significantly increased in 12 (34.3%) patients with oligoasthenozoospermia. **Conclusion** Aberrant methylation of *DAZL* gene promoters is associated with male infertility, and it may be a biomarker of human spermatogenesis defect.

【Key words】 Male infertility; *DAZL* gene; Oligoasthenozoospermia; DNA methylation; Bisulfite genomic sequencing PCR

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·实验研究·

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蛋白 PTEN 通过调节子宫内腔上皮细胞极性影响胚胎着床

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【摘要】 目的 探讨人第 10 号染色体缺失的磷酸酶及张力蛋白同源基因 (phosphatase and tensin homolog deleted on chromosome 10, PTEN) 对子宫内腔上皮细胞极性的调控及对胚胎着床的影响。方法 通过实时荧光定量 PCR、Western blotting、细胞免疫荧光实验比较非容受态子宫内腔上皮细胞 HEC-1A 与容受态子宫内腔上皮细胞 RL95-2 之间 PTEN 的表达及定位差异; PTEN 干扰质粒转染 HEC-1A 细胞, 检测紧密连接相关蛋白质表达水平, 透射电子显微镜检测紧密连接结构, Transwell 实验检测细胞运动能力, 与绒毛膜癌细胞 JAR 共培养检测 HEC-1A 细胞与 JAR 细胞之间的黏附水平; 向体外培养的 HEC-1A 细胞分别加入二甲基亚砜、17 β -雌二醇、孕酮、17 β -雌二醇+孕酮, 检测卵巢激素对 PTEN 表达的影响。结果 相较 HEC-1A 细胞, RL95-2 细胞 *PTEN* 基因及蛋白质表达水平均显著降低 (P 均=0.003); PTEN 主要定位于 RL95-2 细胞核, 而在 HEC-1A 细胞中, PTEN 主要定位于细胞质; 与质粒载体对照组相比, 敲降 *PTEN* 基因后, HEC-1A 细胞紧密连接相关蛋白 ZO-1、Occludin 和 Claudin-4 表达水平显著降低 ($P<0.001$, $P=0.038$, $P<0.001$), 细胞间紧密连接长度降低 ($P=0.046$), 迁移与侵袭能力增强 (P 均<0.001), 与 JAR 细胞之间黏附率增强 ($P=0.016$); 与空白对照组 (二甲基亚砜组) 相比, 17 β -雌二醇组、孕酮组及 17 β -雌二醇+孕酮组的 PTEN 蛋白表达水平均显著降低 (P 均<0.001), 17 β -雌二醇+孕酮组的 PTEN 蛋白表达水平显著低于 17 β -雌二醇组和孕酮组 (P 均=0.001), 孕酮组与雌二醇组的 PTEN 蛋白表达水平差异无统计学意义 ($P>0.05$)。结论 不同容受状态的子宫内腔细胞 PTEN 表达存在差异, 雌二醇和孕酮可能通过抑制 PTEN 在子宫内腔的表达, 进一步调控子宫内腔上皮细胞间紧密连接结构及细胞极性, 从而增强子宫内腔容受性。

【关键词】 PTEN; 极性; 紧密连接; 子宫内腔上皮

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PTEN affects embryo implantation by regulating the polarity of endometrial luminal epithelial cells

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【Abstract】 Objective To investigate the regulation of phosphatase and tensin homolog deleted on chromosomes 10 (PTEN) in the polarity of endometrial lumen epithelial cells and their effects on embryo implantation. **Methods** The differences in PTEN expression and localization between non-receptive endometrial epithelial cells (HEC-1A) and receptive endometrial epithelial cells (RL95-2) were compared by qRT-PCR, Western blotting and immunofluorescence. After the transfection of PTEN siRNA into HEC-1A cells, tight junction (TJ) related proteins, TJ structure, cell motility and adhesive capacity with choriocarcinoma cells (JAR) were detected respectively by Western blotting, transmission electron microscope (TEM), Transwell assay and adhesion assay. After dimethylsulfoxide (DMSO), 17 β -estradiol, progesterone, and 17 β -estradiol+progesterone were respectively added into HEC-1A *in vitro*, the PTEN protein expression were detected by Western blotting to study the effect of ovarian hormone on PTEN. **Results** Compared with HEC-1A cells, the gene and protein expression levels of PTEN in RL95-2 cells were significantly reduced (both $P=0.003$), PTEN was mainly located in the nucleus of RL95-2 and cytoplasm of HEC-1A. Compared with the plasmid vector control group, the expression level of TJ related proteins (ZO-1, Occludin, Claudin-4) in HEC-1A cells was significantly reduced ($P<0.001$, $P=0.038$, $P<0.001$), the length of TJ between cells were reduced ($P=0.046$), the ability of migration and invasion were enhanced (both $P<0.001$), and the adhesion rate to JAR cells was enhanced after knockdown of PTEN in HEC-1A ($P=0.016$). Compared with the DMSO blank group, the expression level of PTEN protein in 17 β -estradiol group, progesterone group and 17 β -estradiol+progesterone group were significantly reduced (all $P<0.001$), the expression level of PTEN protein in 17 β -estradiol+progesterone group was significantly lower than that in both 17 β -estradiol group and progesterone group (both $P=0.001$), and there was no difference in the expression level of PTEN protein between progesterone group and 17 β -estradiol group. **Conclusion** There are differences in the expression of PTEN in endometrial cells with different receptivity states. 17 β -estradiol and progesterone may regulate the TJ structure and cell polarity of endometrial epithelial cells by inhibiting the expression of PTEN in endometrial luminal epithelium, thereby enhancing the endometrial receptivity.

【Key words】 PTEN; Polarity; Tight junction; Endometrial luminal epithelial cells

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中国使用精子库冷冻精液助孕对子 代出生缺陷影响的 meta 分析

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【摘要】 目的 通过 meta 分析方法评价使用精子库冷冻精液助孕出生的子代出生缺陷情况, 为精液冷冻在辅助生殖中应用的安全性和可靠性提供科学依据。方法 检索中国期刊全文数据库 (CNKI)、万方数据库 (Wanfang)、维普中文科技期刊数据库 (VIP)、中国生物医学文献数据库 (CBMDisc) 及 PubMed 数据库截止至 2019 年 10 月 1 日所有收录的使用精子库冷冻精液行辅助生殖中有关子代出生缺陷的文献资料, 严格按照纳入与排除标准筛选文献、提取资料, 并根据 STROBE 声明中横断面研究评价标准进行文献质量评价。结果 最终共纳入 13 篇文献, 总样本量为 33 398 例, 出生缺陷率为 1.09% (95% CI=0.85%~1.32%), 低于国家卫健委 (原卫生部) 发布的检测数据 (1.53%, $P<0.001$)。供精人工授精 (artificial insemination by donor, AID) 组出生缺陷率为 1.06% (95% CI=0.78%~1.35%), 体外受精 (in vitro fertilization, IVF) 组为 0.60% (95% CI=0.03%~1.22%), 卵胞质内单精子注射 (intracytoplasmic sperm injection, ICSI) 组为 1.35% (95% CI=0.06%~2.75%), 差异无统计学意义 ($P=0.785$)。出生缺陷类别中, 以循环系统先天性畸形发生率最高, 其次为肌肉骨骼系统先天性畸形和变形、泌尿生殖系统先天性疾病等。结论 使用精子库冷冻精液助孕未增加子代出生缺陷的风险, 但受纳入研究的质量限制, 上述结论尚需开展更多高质量研究予以验证。

【关键词】 冷冻精液; 生殖技术, 辅助; 出生缺陷; meta 分析

Effect of frozen semen from sperm bank on birth defects in assisted reproduction technology in China: a meta-analysis

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【 Abstract 】 Objective To evaluate the incidence of birth defects in offspring using frozen semen from sperm banks by meta-analysis, to provide scientific evidence for the safety and reliability of frozen semen in assisted reproductive technology (ART). **Methods** China National Knowledge Infrastructure (CNKI), Wanfang Digital Database (Wanfang), VIP Citation Database (VIP), CBMDisc and PubMed were searched about birth defects using frozen semen in ART since the establishment to October 1, 2019. Literatures were screened according to the predefined inclusion and exclusion criteria and evaluated based on the STROBE statement. **Results** Thirteen studies with 33 398 cases were included, the rate of birth defects using frozen semen was 1.09% (95% CI=0.85%–1.32%), lower than that published by the Chinese Ministry of Health (1.53%, $P<0.001$). The rate was 1.06% (95% CI=0.78%–1.35%) in artificial insemination by donor (AID), 0.60% (95% CI=0.03%–1.22%) in *in vitro* fertilization (IVF) and 1.35% (95% CI=0.06%–2.75%) in intracytoplasmic sperm injection (ICSI), the difference was not statistically significant ($P=0.785$). Among the birth defects, the cardiovascular system had the highest rate, followed by the central nervous system and musculoskeletal system and congenital urogenital system and so on. **Conclusion** ART with cryopreserved donor sperm does not increase the risk of birth defects. However, more studies with large sample sizes are needed to confirm this conclusion because some papers with low study quality were included in this study.

【 Key words 】 Frozen semen; Reproductive technology, assisted; Birth defects; Meta-analysis

·现场调查·

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流产后关爱服务对未育青少年女性避孕措施选择及重复流产的影响

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【摘要】 目的 了解未育青少年人工流产及避孕现状, 探讨流产后关爱 (post-abortion care, PAC) 服务对未育青少年女性避孕措施选择及重复人工流产的影响。方法 回顾性研究 2018 年 1 月至 12 月期间广东省妇幼保健院门诊进行人工流产的未育青少年女性患者, 通过 PAC 咨询和随访, 比较手术前后避孕及重复人工流产等状况。结果 ①未育青少年人工流产 1137 人次, 占同期青少年人工流产总数的 85.30% (1137/1333), 占人工流产总数的 29.51% (1137/3853); 术前有人工流产史者占 23.39% (266/1137), 人工流产总次数 ≥ 3 次者占 5.54% (63/1137)、半年内重复人工流产 (即 ≥ 2 次人工流产) 者占 2.73% (31/1137)、1 年内重复人工流产者占 6.86% (78/1137)。②PAC 后选择高效避孕方法较术前显著增加 (2.73% 比 84.43%, $P<0.001$), 其中复方口服避孕药 (combined oral contraceptive, COC) 和宫内节育器 (intrauterine device, IUD) 使用率均显著增加 (2.73% 比 83.46%, $P<0.001$; 0 比 0.97%, $P=0.001$), 使用 IUD 的已婚人数多于未婚人数 (5.71% 比 0.86%, $P=0.047$); 术后 3 个月、6 个月、12 个月 COC 续用率逐渐下降 (83.01%、5.95%、2.46%), 而 IUD 续用率相对稳定 (0.97%、1.14%、1.23%)。③PAC 后半年及 1 年内重复人工流产率与术前比较显著下降 (1.26% 比 2.73%, $P=0.022$; 3.70% 比 6.86%, $P=0.003$)。结论 未育青少年女性重复人工流产率高, 高效避孕措施使用率低, PAC 能显著提高高效避孕措施即时落实率。尚需进一步提高 IUD 即时落实率和 COC 续用率。

【关键词】 青少年; 流产后关爱; 高效避孕方法; 重复人工流产
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Influence of post-abortion care services on contraceptive choice and repeated abortion of nonparous adolescent women

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【Abstract】 Objective To understand the current status of abortion and contraception among nonparous adolescent women and explore the influence of post-abortion care (PAC) services on their contraceptive choice and repeated abortion. **Methods** A retrospective study was conducted on the nonparous adolescent women who had undergone induced abortion in outpatient clinics of Guangdong Women's and Children's Hospital from January to December 2018 was recruited. Through PAC consultation and follow-up, their contraceptive options and the incidence of repeated abortions before and after surgery were compared. **Results** 1) There were 1137 cases of induced abortion among nonparous adolescent women, accounting for 85.30% (1137/1333) of the total number of adolescent abortions, 29.51% (1137/3853) of the total number of abortions during

the same period, among which 23.39% (266/1137) had abortion history before surgery, 5.54% (63/1137) had abortion ≥ 3 times, 2.73% (31/1137) had repeated abortion (≥ 2 times within 1 year) within half a year, and 6.86% (78/1137) had abortion ≥ 2 times within 1 year. 2) There was a significant increase in the choice of high-efficiency contraceptive methods after PAC compared with that before surgery (2.73% vs. 84.43%, $P < 0.001$), in which the use of combined oral contraceptive (COC) and intrauterine device (IUD) increased significantly (2.73% vs. 83.46%, $P < 0.001$; 0 vs. 0.97%, $P = 0.001$), and the number of married women using IUD was higher than that of unmarried women (5.71% vs. 0.86%, $P = 0.047$). On the other hand, the rate of continued use of COC at 3, 6, and 12 months of post-operative nonparous adolescent women gradually decreased (83.01%, 5.95%, 2.46%), while the rate of continued use of IUD remained stable (0.97%, 1.14%, 1.23%). 3) The repeated induced abortion rate among nonparous adolescent women in the half of a year and one year after PAC significantly decreased compared with that before PAC (1.26% vs. 2.73%, $P = 0.022$; 3.70% vs. 6.86%, $P = 0.003$). **Conclusion** Nonparous adolescent women have a higher rate of repeated abortions, while a lower rate of the use of high-efficiency contraceptive methods. PAC services can significantly improve the immediate implementation rate of high-efficiency contraceptives, and it is necessary to further increase the immediate implementation rate of IUD and the continued use rate of the COC.

【Key words】 Nonparous adolescent women; Post-abortion care; High-efficiency contraceptive methods; Repeated induced abortion

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·个案报道·

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罕见 P 血型不合致反复流产 1 例

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【摘要】 目的 旨在为反复流产的诊治提供新方向。方法 回顾性分析 1 例反复流产患者的临床资料，该患者血型不规则抗体阳性，最终确定血型为 p 血型。考虑其反复流产与罕见血型关系密切，且已中期妊娠，胎盘低置，经多学科会诊后，制定预存式自体备血方案。结果 该例患者引产过程顺利。结论 排除常见流产原因后，产科医生要对孕妇的不规则抗体进行筛查，并为需要备血的稀有血型孕妇围生期备血提供建议，可行预存式自体备血作为出血紧急预案之一。

【关键词】 反复流产； P 血型不合； 预存式自体备血

Spontaneous abortion caused by rare maternal-fetal P blood group incompatibility: a case report

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【Abstract】 Objective To provide a new direction for the diagnosis and treatment of recurrent spontaneous abortion. **Methods** The clinical data of one patient with repeated abortion were retrospectively analyzed. The patient's blood type was finally confirmed to be the rare p blood type. Considering that the patient was in the second trimester and had low-implantating placenta, a pre-stored autologous blood preparation scheme was developed after multidisciplinary consultation. **Results** The induction of labor was successful in this case. **Conclusion** After excluding the common causes of abortion, obstetricians should screen pregnant women for irregular antibodies in blood, and also provide suggestions for perinatal blood preparation for rare blood group pregnant women. It is feasible to adopt pre-stored autologous blood preparation as one of the emergency transfusion pre-plans.

【Key words】 Recurrent spontaneous abortion; P blood-group incompatibility; Pre-stored autologous blood preparation

·综述·

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冻融单囊胚移植胚胎选择策略的研究进展

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【摘要】 现代体外受精-胚胎移植 (*in vitro* fertilization-embryo transfer, IVF-ET) 的新目标是选择和移植 1 枚最具发育潜能的胚胎, 从而获得健康的单胎妊娠。为了实现这一目标, 需要单胚胎移植并且达到最大化的单胎活产率。由于冻融囊胚移植较新鲜囊胚移植活产率高, 且胚胎和子宫内膜之间的同步性更好, 因此选择最优的冷冻单囊胚进行移植至关重要。本文综述了冻融单囊胚移植的潜在益处、单囊胚选择的非侵入性策略及不同发育速度囊胚的取舍。

【关键词】 单囊胚移植; 冻融囊胚; 囊胚形态; 无创染色体筛查; 胚胎选择

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Research progress of embryo selection strategies for freeze-thaw single blastocyst transfer

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【Abstract】 The new objective of modern *in vitro* fertilization-embryo transfer (IVF-ET) is to select and transfer the most competent embryo for a healthy single pregnancy. In order to achieve this goal, it is necessary to transfer single embryo and maximize the live birth rate of single embryo. Since freeze-thaw blastocyst transfer has a higher live birth rate than fresh blastocyst transplantation and better synchronization between embryo and endometrium, it is essential to select the best frozen single blastocyst for transfer. This paper reviews the potential advantages of freeze-thaw single blastocyst transfer, the non-invasive strategies for single embryo selection and the option of blastocysts at different development rates.

【Key words】 Single blastocyst transfer; Freeze-thaw blastocyst; Blastocyst morphology; Noninvasive chromosome screening; Embryo selection

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·综述·

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卵巢交界性肿瘤患者进行辅助生育治疗的研究进展

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【摘要】 卵巢交界性肿瘤（borderline ovarian tumors, BOTs）是一种生物学行为介于卵巢良、恶性肿瘤之间的特殊类型，好发于生育年龄女性，预后较好，合并不孕率较高，BOTs 患者行保留生育功能手术可行，早期、无组织学高危因素的 BOTs 术后行辅助生殖技术（assisted reproductive technology, ART）治疗可行，生育咨询应成为 BOTs 临床管理的一个组成部分，对 BOTs 术后不孕症或不孕高危因素患者应尽早向生殖医生寻求合适的助孕治疗。本文围绕 BOTs 与保留生育功能手术及 ART 的安全性展开综述。

【关键词】 卵巢交界性肿瘤； 生殖技术，辅助； 生育力保存
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Research progress of borderline ovarian tumors in patients with assisted reproductive treatment

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【Abstract】 Borderline ovarian tumors (BOTs) are characterized by the histopathologic feature and biologic behavior which intermediate between clearly benign and frankly malignant ovarian tumors. BOTs are more common in younger women, and most patients are diagnosed in the early stage and with infertility. Fertility sparing surgery (FSS) is safety and beneficial for women with BOTs who desire to maintain their fertility. Assisted reproductive technology is safety and beneficial for women with BOTs in early stage and without any histological high-risk criterion. Fertility counselling should become an integral part of the clinical management of women with BOTs. For BOTs patients with infertility or high risk factors of infertility after FSS operation, it is necessary to seek appropriate treatment from reproductive doctors as early as possible. This article reviews the safety of BOTs, fertility sparing surgery and assisted reproductive treatment.

【Key words】 Borderline ovarian tumors; Reproductive technology, assisted; Fertility preservation

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异常 DNA 甲基化与复发性流产关系的研究进展

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【摘要】 复发性流产 (recurrent spontaneous abortion, RSA) 是生殖育龄期女性的常见疾病, 其发病机制尚不完全清楚。近年来, 随着表观遗传学领域的深入研究, DNA 甲基化逐渐成为 RSA 病理生理机制的新视角。研究表明, DNA 甲基化修饰调控与 RSA 密切相关, DNA 甲基化异常及其引起的印记障碍、蜕膜相关基因表达失调、精子缺陷以及免疫系统异常都直接或间接地影响胚胎的着床、生长及发育过程, 最终导致 RSA 的发生。现阐述 DNA 甲基化在 RSA 发病中的作用及其调控途径的研究进展。

【关键词】 表观遗传; DNA 甲基化; 复发性流产; 胚胎发育

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Research progress on the relationship between abnormal DNA methylation and recurrent spontaneous abortion

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【Abstract】 Recurrent spontaneous abortion (RSA) is a common disease in women of reproductive age, and the pathogenesis is not fully understood. In recent years, with in-depth research in the field of epigenetics, DNA methylation has gradually become a new perspective on the pathophysiology of RSA. Studies have shown that the regulation of DNA methylation modification is closely related to RSA. Abnormal DNA methylation and its imprinting disorders, dysregulated gene expression disorders, sperm defects and immune system abnormalities directly or indirectly affect embryo implantation. The growth and development process eventually lead to the occurrence of RSA. The role of DNA methylation in the pathogenesis of RSA and its regulatory pathways are reviewed.

【Key words】 Epigenetics; DNA methylation; Recurrent spontaneous abortion; Embryonic development

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·综述·

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炎症因子对卵泡发育的影响

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【摘要】 白细胞介素(interleukin, IL)-1家族、IL-6、肿瘤坏死因子(tumor necrosis factor, TNF)- α 、粒细胞-巨噬细胞集落刺激因子(granulocyte macrophage-colony stimulating factor, GM-CSF)等炎症因子所介导的生理性炎症反应参与卵泡发育、成熟及排卵过程, 炎症因子异常表达引发病理性炎症反

应，可导致排卵障碍及不孕，主要见于多囊卵巢综合征（polycystic ovary syndrome, PCOS）、子宫内膜异位症（endometriosis, EMS）、早发性卵巢功能不全（premature ovarian insufficiency, POI）、肥胖、甲状腺功能减退等疾病。本文围绕炎症因子对卵泡发育的生理作用以及在不同疾病中影响卵子发育的可能机制进行阐述，以期对排卵障碍性不孕的诊疗提供帮助。

【关键词】 炎症； 细胞因子类； 卵泡； 生长； 发育

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Effect of inflammatory cytokines on follicular development

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【 Abstract 】 The physiological inflammatory response mediated by inflammatory cytokines such as interleukin (IL)-1 family, IL-6, tumor necrosis factor (TNF)- α , granulocyte macrophage colony stimulating factor (GM-CSF) is involved in follicular development, maturation and ovulation. The abnormal expression of inflammatory cytokines causes pathological inflammatory response, which can lead to ovulation disorders and infertility, was mainly observed in polycystic ovary syndrome (PCOS), endometriosis (EMS), premature ovarian insufficiency (POI), obesity, hypothyroidism and other diseases. This paper focuses on the physiological effect of inflammatory cytokines on follicular development and the possible mechanism of affecting the development of oocytes in different diseases, in order to provide help for the diagnosis and treatment of ovulatory dysfunctional infertility.

【 Key words 】 Inflammation; Cytokines; Ovarian follicle; Growth; Development

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