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脱氢表雄酮对卵巢储备功能低下患者的胚胎质量及卵泡液中标志物的作用

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目的 探讨脱氢表雄醇(DHEA)对于卵巢储备功能低下(DOR)患者胚胎质量及卵泡液标志物的影响。方法 采用前瞻性随机对照研究将 116 名 DOR 患者按照 1:1 随机分为 DHEA 组与对照组。DHEA 组 58 名患者, 给予 DHEA 25 mg/次, tid, 用药 12 周。对照组 58 名患者直接进入体外受精(IVF)周期。比较两组的 IVF 参数(获卵数、MII 卵数、卵裂数、有效胚胎数、优质胚胎数和临床妊娠率)并利用酶联免疫吸附法(ELISA)检测两组卵泡液中的抗苗勒管激素(AMH), 胰岛素样生长因子(IGF)-1 的含量及蛋白免疫印迹法(Western blotting assay)检测骨形态发生蛋白(BMP)-15 及生长分化因子(GDF)-9 在卵泡液中的表达。结果 DHEA 组的有效胚胎数(2.0 ± 1.3)及优质胚胎数(1.4 ± 1.1)明显多于对照组(1.5 ± 1.2, \( P = 0.018 \); 1.0 ± 1.0, \( P = 0.033 \)), 卵泡液样本中的 AMH([2.83 ± 1.14] μg/L)及 IGF-1([94.02 ± 38.28] μg/L) 的含量明显高于对照组([1.37 ± 0.55] μg/L, \( P = 0.000 \); (74.03 ± 25.46) μg/L, \( P = 0.004 \) ), Western blotting 显示 DHEA 组的 BMP-15 蛋白的相对表达量明显增高(\( P < 0.000 1 \) ), 但是 GDF-9 的相对表达量在两组中无统计学差异(\( P = 0.987 \) ), 临床妊娠率在两组中也未见统计学差异(\( P = 0.223 \) )。结论 DOR 患者在 IVF 周期前进行 DHEA 预处理可以提高优质胚胎数, 这可能与卵泡液环境中的相关标志物(AMH, IGF-1 和 BMP-15)含量的增加有关。

【关键词】 脱氢表雄酮(DHEA); 卵巢储备功能低下(DOR); 体外受精(IVF); 骨形态发生蛋白(BMP)-15

【基金项目】 上海市卫计委青年基金项目(20134Y096)
Effect of dehydroepiandrosterone supplementation on the embryo quality and follicular fluid markers in patients with diminished ovarian reserve
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【Abstract】Objective  To examine the effect of the dehydroepiandrosterone (DHEA) supplementation on the embryo quality and the levels of follicular fluid markers in diminished ovarian reserve (DOR) patients for in vitro fertilization (IVF).

Methods  This was a prospective randomization controlled trial. One hundred and sixteen DOR patients were randomized 1：1 into two groups. The DHEA group (n=58) received DHEA 25 mg/times, tid for 12 weeks and control group (n=58) entered the IVF cycle directly. IVF parameters including the number of retrieved oocytes, matured oocytes, cleaved embryos, available embryos, good-quality embryos and clinical pregnancy rate were compared between the two groups. Follicular fluid anti-Müllerian hormone (AMH), insulin growth factor (IGF)-1 were tested by ELISA and the expression levels of bone morphogenetic protein (BMP)-15 and growth differentiation factor (GDF)-9 were tested by Western blotting assay.

Results  The number of available embryos (2.0±1.3) and good-quality embryos (1.4±1.1) were significantly increased in DHEA group than in control group (1.5±1.2, P=0.018; 1.0±1.0, P=0.033). AMH level in follicular fluid [(2.83±1.14) μg/L], IGF-1 concentration [(94.02±38.28) μg/L] were significantly higher in DHEA group than in the control [(1.37±0.55) μg/L, P=0.000; (74.03±25.46) μg/L, P=0.004]. Western blotting showed the expression levels of BMP-15 were higher in DHEA group (P<0.000 1), but GDF-9 was not significantly different (P=0.987). However, the clinical pregnancy rates were also not significant between the two groups (P=0.223).

Conclusion  In women with DOR undergoing treatment with IVF, pre-treatment with DHEA could increase the number of good-quality embryos, which may be associated with the increase level of AMH, IGF-1 and BMP-15 in follicular fluid.

【Key words】 Dehydroepiandrosterone (DHEA); Diminished ovarian reserve (DOR); In vitro fertilization (IVF); Bone morphogenetic protein (BMP)-15

Fund program: Shanghai Municipal Commission of Health and Family Planning (20134Y096)
微刺激全部胚胎冷冻方案在常规体外受精-胚胎移植失败的卵巢低反应患者的中的应用

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【摘要】目的 探讨微刺激全部胚胎冷冻方案在常规体外受精 / 卵泡液内单精子显微注射 - 胚胎移植 (IVF/ICSI-ET) 方案失败的卵巢低反应(POR) 患者中的应用价值。方法 对 196 例 IVF/ICSI-ET 应用常规促排卵方案在 POR 放弃周期或移植失败后改用微刺激方案的 402 个周期进行回顾性分析。比较前、后 2 次不同促排卵方案的临床和实验室指标。结果 402 个微刺激周期中 32 个周期取消。周期取消率为 7.96%, 370 周期获得卵母细胞。平均获卵数(2.2 ± 1.5)个, 共 233 个周期有胚胎冷冻, 胚胎冷冻率为 57.96%, 共 194 个周期进行了 ET, 临床妊娠 74 例, 早期自然流产 6 例, 起始周期累积妊娠率为 37.75%(74/194), 冻融胚胎移植 (FET) 周期临床妊娠率 38.14%(74/194), 其中 ≤ 37 岁组 FET 周期的临床妊娠率(50.89%) 明显高于 >37 岁组(20.73%)(P<0.05)。微刺激方案的临床和实验室指标均显著优于常规长方案。结论 微刺激全部胚胎冷冻方案对常规方案 IVF/ICSI-ET 治疗失败的 POR 患者具有疗程短、刺激剂量小、获卵率高、可利用胚胎率高、周期取消率低等特点, 对于该类患者再次助孕可考虑微刺激方案。

【关键词】 微刺激方案; 卵巢低反应(POR); 体外受精 / 卵泡液内单精子显微注射 - 胚胎移植 (IVF/ICSI-ET)
Application of mild stimulation protocol in poor responders after failure of routine in vitro fertilization-embryo transfer
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Objective To explore the clinical value of mild stimulation protocol applied in poor ovarian responders after failure of routine in vitro fertilization/intracytoplasmic sperm injection-embryo transfer (IVF/ICSI-ET).

Methods A total of 196 poor ovarian responders were initially taken by pituitary down regulation protocols. After unsuccessful pregnancy, another 402 mild stimulation protocols were applied. A retrospective study was performed to compare the data and clinical outcomes between the two protocols of the same patients.

Results Totally 32 cycles were canceled in the total 402 mild stimulation cycles, the cancelleration rate was 7.96%. Among 370 cycles obtained oocytes, the mean number of oocytes obtained was 2.2 ± 1.5. A total of 233 cycles owned frozen embryos, fertilization rate was 57.96%. Seventy-four clinical pregnancies were got in the 194 transfer cycles, 6 were aborted, the frozen rate was 27.68% (98/354), the pregnancy rates per starting cycles and per transfer cycle was 37.75% (74/196) and 38.14% (74/194), respectively. Clinical and laboratory indexes were better in mild stimulation than routine stimulating ovulation cycles.

Conclusion Mild stimulation protocol is cheaper, easier to use, short stimulation days, less stress and produces less complications compared with the standard protocol when used in poor responders after failure of routine IVF-ET.

Key words Mild stimulation; Poor ovarian response (POR); in vitro fertilization/intracytoplasmic sperm injection-embryo transfer (IVF/ICSI-ET)
冻融囊胚移植周期生化妊娠相关因素分析

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【摘要】目的 分析冻融囊胚移植周期中导致生化妊娠的相关因素。方法 回顾性分析行冻融囊胚移植后生化妊娠的 70 个周期的临床资料, 以同期冻融囊胚移植后正常宫内妊娠的 336 个周期为对照, 比较影响生化妊娠相关因素。结果 生化妊娠组年龄比正常宫内妊娠组大, 合并亚临床甲状腺功能减退(SCH) 及未治疗或治疗后仍不正常的患者生化妊娠组更多, 差异有统计学意义(P<0.05)。结论 重视高龄患者、胚胎移植前纠正 SCH, 有助于降低冻融囊胚移植周期生化妊娠发生率。

【关键词】 冻融囊胚移植; 生化妊娠; 年龄; 亚临床甲状腺功能减退(SCH)
Analysis of the influencing factors on the biochemical pregnancy after frozen-thawed blastocyst transfer

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Objective To analysis the influencing factors on the biochemical pregnancy after frozen-thawed blastocyst transfer. Methods The data of 70 biochemical and 336 intrauterine pregnancy cycles from January 2014 to December 2016 were retrospectively analyzed. Results There were significant differences in female age, the occurrence of subclinical hypothyroidism (SCH) between the biochemical pregnancy group and intrauterine pregnancy group (P<0.05). Conclusion Attention to aged patients and controlling SCH before frozen-thawed blastocyst transfer will help reduce the incidence of biochemical pregnancy.

Key words Frozen-thawed blastocyst transfer; Biochemical pregnancy; Age; Subclinical hypothyroidism (SCH)
全部胚胎冷冻对不同促排卵方案患者临床应用的探讨

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【摘要】目的 分析不同促排卵方案新鲜胚胎移植和冻融胚胎移植的临床妊娠结局。方法 回顾性分析行胚胎移植的525个周期患者的临床资料，其中253个周期为新鲜胚胎移植周期，272个周期为同期的复苏胚胎移植周期。纳入的促排卵方案包括促性腺激素释放激素激动剂(GnRH-a)长方案组(A组)和GnRH-a短方案组(B组)。分别比较两组中新鲜胚胎移植和冻融胚胎移植(FET)的妊娠结局。以及新鲜胚胎移植周期和复苏胚胎移植周期中2种方案妊娠结局。结果 A组中，新鲜胚胎移植周期(A1组)和FET周期(A2组)的临床妊娠率分别为45.95%和47.71%(P>0.05)；B组中，新鲜胚胎移植周期(B1组)和FET(B2组)的临床妊娠率分别为27.94%和46.30%(P<0.05)；A1组和B1组的受精率和可用胚胎率组间统计学差异(P>0.05)。A组的平均获卵数、临床妊娠率和胚胎种植率显著高于B组(P<0.05)；A2组和B2组的临床妊娠率和胚胎种植率均统计学差异(P>0.05)。结论 FET并不能显著改善长方案患者的临床妊娠结局，但可显著提高短方案组的临床妊娠率。提示短方案患者可考虑采用全部胚胎冷冻。

【关键词】 冻融胚胎移植(FET); 短方案; 胚胎种植率; 妊娠率

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Investigation of the clinical application of whole embryo freezing to different ovulation hyper-stimulation protocols  Qiu Xuemei, Wang Lei, Ding Chen, Zhao Shuqin
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【Abstract】Objective  To analyze the clinical pregnancy rate of different controlled ovarian hyperstimulation (COH) protocols in fresh embryo transfer (ET) and frozen-thawed embryo transfer (FET) cycles and to investigate the clinical application value of whole embryo cryopreservation. Methods  A total of 525 patients which were performed embryo transfer were retrospectively analyzed, including 253 fresh ET cycles and 272 FET cycles. Patients were divided into gonadotrophin-releasing hormone agonist (GnRH-a) long protocol group (group A) and GnRHa short protocol group (group B). The pregnancy outcome of fresh ET and FET were analyzed between the two groups. Furthermore, the efficacy of induced ovulation and pregnancy outcome in fresh ET cycles and the pregnancy outcome in FET cycles of the two COH protocols were compared. Results  In group A, the clinical pregnancy rate was 45.95% and 47.72% (P>0.05) respectively for fresh embryo transfer and FET cycles, which was 27.94% and 46.30% (P<0.05) respectively in group B. In fresh embryo transfer cycles, there was no significant difference in the fertility rate and the available embryo rate between the two groups, but the average number of oocytes retrieved, the clinical pregnancy rate and the embryo implantation rate were significantly higher (P<0.05) in group A than in group B. There were no significant differences in the clinical pregnancy rate and the embryo implantation rate in FET cycles between group A and group B (P>0.05). Conclusion  FET did not significantly improve the clinical pregnancy outcome of patients with GnRH-a long protocol, and FET can increase the clinical pregnancy rate in patients with GnRH-a short protocol compared with the fresh embryo transfer. Patients with GnRH-a short protocol could be considered to use whole embryo cryopreservation strategy.

【Key words】 Frozen-thawed embryo transfer (FET); Gonadotrophin-releasing hormone agonist (GnRH-a) short protocol; Embryo implantation rate; Pregnancy rate

Fund program: Natural Science Foundation of Shandong Province (2015ZRA04005)
临床研究

宫腔镜子宫内膜微刺激术后再次冻融胚胎移植的临床结局

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【摘要】目的  探讨宫腔镜子宫内膜微刺激术对再次移植冻融胚胎患者临床结局的影响。方法  选取2015年1月—2016年8月在本院行体外受精(IVF)助孕首次移植治疗失败的患者共281例,随机分为研究组(A组)和对照组(B组)。A组129例,月经干净后第3~7日进行宫腔镜子宫内膜微刺激术;B组152例,第2次移植前未行手术。统计分析冻融胚胎移植(FET)的妊娠结局。结果  (1) A、B两组间患者年龄、
不孕年限、基础性激素、体质量指数、黄体酮转化日内膜厚度、移植胚胎数、优质胚胎数、异位妊娠率、多胎率、早期流产率相比较,差异无统计学意义(P>0.05)。② A组的临床妊娠率和着床率分别是58.1%、34.0%,显著高于B组(47.4%、27.6%)(P<0.05)。进一步分析多因素Logistic回归分析显示,宫腔镜子宫内膜微刺激术能够显著增加临床妊娠的几率(OR=1.50, 95% CI=1.12~2.43), 而对异位妊娠、多胎妊娠及早期流产的发生无明显影响。结论  宫腔镜子宫内膜微刺激术属微创手术,并发症少,手术方便快捷, 能更直观评价患者的宫腔内情况, 并且通过对照子宫内膜局部微刺激,改善内膜容受性, 提高着床率、妊娠率。故宫腔镜子宫内膜微刺激术值得推广。

【关键词】 宫腔镜; 子宫内膜微刺激术; 冻融胚胎移植(FET); 子宫内膜容受性; 体外受精-胚胎移植(IVF-ET)

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Clinical outcome of hysteroscopic endometrium local injury on patients who suffered from implantation failure in previous frozen-thawed embryo transfer
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【Abstract】Objective To explore the effects of hysteroscopic endometrium local injury on clinical outcome of patients who suffered from implantation failure in previous frozen-thawed embryo transfer (FET).
Methods Totally 281 patients who suffered from implantation failure in previous FET were divided into two groups randomly. The patients in group A (129 cases) were treated by hysteroscopic endometrial local injury 3–7 d after menstruation clean, 152 cases in group B (control group) were not treated by endometrium local injury. Statistical analysis of FET pregnancy outcome was performed to understand the difference between two groups. Results No significant differences were found between two groups in patients’ age, duration of infertility, the levels of basal sex hormones, body mass index (BMI), thickness of endometrium on progesterone conversion day, number of transferred embryos, quality embryo rate, ectopic pregnancy rate, multiple pregnancy rate, and early miscarriage rate. Patients in group A gained significantly higher clinical pregnancy rate and implantation rate than group B. Multiple regression analysis showed that hysteroscopy endometrial local injury significantly improved the occurrence of clinical pregnancy ($OR=1.50$, $95\%\ CI=1.12$–2.43), whereas other parameters like ectopic pregnancy rate, multiple pregnancy rate, and early miscarriage rate were not obviously affected. Conclusions Hysteroscopy endometrium local injury is a minimally invasive surgery, less complications, convenient and quick operation. By executing this operation, we could make more accurate evaluation of intrauterine condition for patients, moreover, we could also ameliorate patients situation by improving the endometrial receptivity, obtaining higher clinical pregnancy rate and implantation rate. Therefore, hysteroscopy endometrium local injury was suggested to be executed in clinic operations.

【Key words】Hysteroscopy; Endometrium local injury; Frozen-thawed embryo transfer (FET); Endometrial receptivity; In vitro fertilization-embryo transfer (IVF-ET)

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促排卵启动时间对子宫内膜异位症妇女体外受精妊娠结局的影响

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【摘要】目的 探讨改良超长方案中根据降调后的血清 E2 水平选择合适的促性腺激素(Gn)启动时间在子宫内膜异位症(EMS)妇女体外受精/胚胎移植(IVF/ICSI-ET)的临床应用。方法 对98例IVF/ICSI-ET 周期进行回顾性分析，改良超长方案治疗的65为例为实验组，根据不孕因素分为 A 组(EMS 性不孕)和 B 组(非 EMS 性不孕)，A、B 组均根据血清 E2 水平选择恰当的时机启动 Gn; 另外按常规超长方案治疗的33 例作为对照组(C 组，EMS 性不孕)，比较各组临床指标的差异。结果 ① A 组 Gn 使用总量[(2 330.4 ± 747.8) IU]明显小于 B 组[(3 338.7 ± 1 341.5) IU](P<0.05)，A 组的受精率(77.6%)明显高于 B 组(65.8%)(P<0.05)，获卵数、妊娠率有增加趋势，但无统计学差异(P>0.05)。② A 组 Gn 起始剂量[(192.0 ± 35.3) IU]、使用总量[(2 330.4 ± 747.8) IU]均显著低于 C 组[(228.8 ± 48.9) IU, (2 828.5 ± 1 129.0) IU](P<0.05)，A 组的启动时间[(35.9 ± 7.4) d]显著低于 C 组[(28.0 ± 0.0) d](P<0.05)，A 组获卵数(8.8 ± 4.7)显著高于 C 组(6.1 ± 3.9)(P<0.05)，两组的受精率、优质胚胎率、妊娠率均无统计学差异(P>0.05)。结论 在改良超长方案中，通过监测降调节后的血清 E2 水平，选择恰当的时机启动 Gn，可以在不影响结果的情况下减少 Gn 的用量，特别对于 EMS 患者更明显，是一种经济有效的降调节方案。

【关键词】 改良超长方案; 促性腺激素启动时机; 血清 E2 水平; 子宫内膜异位症(EMS)
Effect of starting time of ovarian stimulation on outcomes of in vitro fertilization in women with endometriosis  

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【Abstract】Objective To investigate the effect of appropriate starting time of gonadotropin (Gn) in modified prolonged protocol on outcomes of in vitro fertilization/intracytoplasmic sperm injection-embryo transfer (IVF/ICSI-ET) in women with endometriosis (EMS). Methods A total of 98 cycles from infertile patients who underwent IVF/ICSI were retrospectively analyzed. The patients were divided into group A (modified prolonged protocol, EMS, n=44), group B (modified prolonged protocol, non-EMS, n=21) and group C (regular prolonged protocol, EMS, n=33). The difference of clinic outcomes was compared and analyzed among the different groups. Results 1) The total dosage of Gn used was lower and the fertilization rate was higher in group A [(2 330.4±747.8) IU, 77.6%] than in group B [(3 338.7±1 341.5) IU, 65.8%], the differences were statistically significant (P<0.05). No statistically significant difference was observed in the number of oocytes retrieved and the clinical pregnancy rate between group A and group B (P>0.05). 2) The initial dosage and total dosage of Gn used in group A [(192.0±35.3) IU, (2 330.4±747.8) IU] was higher than that in group C [(228.8±48.9) IU, (2 828.5±1 129.0) IU], the difference was statistically significant (P<0.05). The number of retrieved oocytes in group A (8.8±4.7) was higher than that in group C (6.1±3.9), the difference was statistically significant (P<0.05). No statistically significant difference was found in the fertilization rate, high-quality embryos rate, clinical pregnancy rate between group A and group C (P>0.05). Conclusion It is a cost-effective controlled ovarian hyperstimulation (COH) protocol for infertile patients with EMS, because the modified prolonged protocol can reduce the dosage of Gn used without affecting the clinical results through monitoring E2 level.  

【Key words】Modified prolonged protocol; Starting time of gonadotropin; Serum E2 level; Endometriosis
女方染色体多态对体外受精-胚胎移植妊娠结局的影响

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【摘要】目的 探讨女方染色体多态性对体外受精-胚胎移植(IVF-ET)结局的影响。方法 回顾性比较 IVF-ET 助孕治疗的女方染色体多态(65 对, 女方多胎组)和正常对照夫妇(160 对, 正常对照组)的妊娠结局。结果 女方多态组与正常对照组患者双原核(2PN)受精率、胚胎率、生化妊娠率均无统计学差异(P>0.05); 然而多态组1PN受精率(8.48%)及多PN受精率(12.50%)均显著高于正常对照组(3.90%, 7.96%) (P<0.01), 卵裂率(89.21%)显著低于正常对照组(98.36%) (P<0.01)。虽然妊娠率比较未见明显差异, 但多态组种植率(23.89%)低于正常对照组(35.40%) (P<0.05)。将不同的多态类型详细分组与正常对照组对比结果显示: 1 号、9 号、16 号染色体易染色质增加组 1PN 受精率(11.36%)及多 PN 受精率(17.02%)均显著高于正常对照组(3.90%, 7.96%) (P<0.01), 卵裂率(87.90%)显著低于正常对照组(98.36%, P<0.01); D/G组随体细胞增加组卵裂率(80.00%)及种植率(17.65%)均低于对照组(98.36%, 35.40%) (P<0.01, P<0.05); 而 9 号染色体臂间倒位[inv(9)]患者各项指标与正常对照组相比无统计学差异。结论 女方染色体多态, 尤其是 1 号、9 号、16 号染色体易染色质增加会导致 IVF 助孕患者异常受精比例增加以及种植率降低; inv(9)对 IVF 临床预后无明影响, 临床可根据患者的多态类型个体化给与遗传咨询指导。

【关键词】 女方染色体多态性, 体外受精-胚胎移植(IVF-ET), 妊娠结局: 1qh+; 9qh+; 16qh+; 9 号染色体臂间倒位[inv(9)]

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Effect of female chromosomal polymorphism on in vitro fertilization and embryo transfer outcomes

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**Abstract**

Objective To explore the effect of female chromosomal polymorphism on in vitro fertilization and embryo transfer (IVF-ET) outcomes.

Methods A retrospective analysis was performed in 65 couples with female chromosomal polymorphism as the study group, and 160 normal karyotype couples as control group. The clinical outcomes including good-quality embryo rate, clinical pregnancy rate, implantation rate and miscarriage rate were compared between the two groups.

Results There were no significant differences between two groups in patient 2 pronucleus (PN) fertilized oocytes rate, good-quality embryo rate, clinical pregnancy rate and biochemical pregnancy rate ($P > 0.05$), but the study group had higher 1PN fertilized oocytes rate (8.48%) and polypronuclear rate (12.50%) and lower cleaved embryos rate (89.21%) than the control (3.90%, 7.96%, 98.36%) ($P < 0.01$). Study group was divided into three subgroups as their polymorphism types and then compared with the control. 1qh+, 9qh+ and 16qh+ subgroup had higher 1PN fertilized oocytes rate (11.36%) and polypronuclear rate (17.02%), and lower cleaved embryos rate (87.90%) than the control (3.90%, 7.96%, 98.36%) ($P < 0.01$); D/G group had lower cleaved embryos rate (80.00%) and implantation rate (17.65%) compared with control group (98.36%, 35.40%) ($P < 0.01$, $P < 0.05$). There were no significant differences between the inv(9) group and the control.

Conclusions Female chromosomal polymorphism, especially 1qh+, 9qh+ and 16qh+ carrier increase abnormal fertilization rate and decrease implantation rate. Chromosome 9 pericentric inversion does not impact IVF outcomes. We should afford individual genetic counseling suggestion according to the polymorphism types.

**Key words** Female chromosomal polymorphism; In vitro fertilization and embryo transfer (IVF-ET); Pregnancy outcome; 1qh+; 9qh+; 16qh+; Chromosome 9 pericentric inversion [inv(9)]

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两种不同胚胎装载技术对体外受精-胚胎移植及冻融胚胎移植临床结局的影响

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【摘要】目的 探讨两种不同胚胎装载技术对体外受精-胚胎移植(IVF-ET)和冻融胚胎移植(FET)临床妊娠率及胚胎种植率的影响。方法 回顾性分析了543个新鲜胚胎移植周期及658个FET周期。根据移植时胚胎载装方法分为A组(含胚培养液体积>周围空气体积)和B组(含胚培养液体积<周围空气体积)。比较两种胚胎载装方法对妊娠结局的影响。结果 新鲜周期中, B组的临床妊娠率(64.52%)显著高于A组(54.62%) (P<0.05), 种植率组间无统计学差异(P>0.05), 但B组明显高于A组。FET周期中卵裂胚胎移植B组的临床妊娠率(49.43%)明显高于A组(38.24%), 但无统计学差异(P>0.05), B组(34.62%)的种植率显著高于A组(23.61%) (P<0.05)。囊胚移植两组的妊娠率和种植率均无统计学差异(P>0.05), 但B组比A组有增高的趋势。结论 胚胎移植时含胚培养液体积>周围空气体积会显著提高IVF-ET和FET的临床妊娠率和种植率。

【关键词】 胚胎装载技术; 体外受精-胚胎移植(IVF-ET); 冻融胚胎移植(FET); 妊娠率; 种植率
Impact of two different embryo loading techniques on pregnancy outcome in in vitro fertilization and frozen-thawed embryo transfer cycles

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Abstract

Objective To evaluate the impact of two different embryo loading techniques on pregnancy rates and implantation rate in in vitro fertilization and embryo transfer (IVF-ET) cycles and frozen-thawed embryo transfer (FET) cycles.

Methods We retrospectively analyzed 543 fresh ET cycles and 658 FET cycles. The patients were placed in group A and group B, group A: the volume of medium containing embryos>air bubble surrounding it; group B: the volume of medium containing embryos<air bubble surrounding it. The pregnancy outcome was compared between the two groups.

Results In fresh ET cycles, the pregnancy rate in group B (64.52%) was significantly higher than that in group A (54.62%) (P<0.05). There was no significant difference of implantation rate in groups A and B, but it was higher in group B than in group A obviously. In FET cycles, the cleavage embryo pregnancy in group B was higher than that in group A obviously, but there was no significant difference (P>0.05). The implantation rate was higher in group B (39.51%) than in group A (26.81%), the difference was significant (P<0.05). There were no significant differences in both pregnancy rate and implantation rate of blastocyst, but it was higher in group B than in group A. Conclusion The volume of medium containing embryos < air bubble surrounding it can significantly improve the pregnancy rate and implantation rate in fresh ET cycles and FET cycles.

Key words Embryo loading techniques; In vitro fertilization-embryo transfer (IVF-ET); Frozen-thawed embryo transfer (FET); Pregnancy rate; Implantation rate
CCL2 通过抑制白细胞介素-24 表达增强人绒毛膜滋养细胞株的细胞活力

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【摘要】目的 探讨白细胞介素-24(interleukin-24, IL-24)对人滋养细胞活力的调节作用。方法 免疫组织化学法检测 IL-24 及其受体(IL-20R1、IL-20R2 和 IL-22R1)在正常早孕期绒毛组织的表达; In-cell Western 法分析重组胸腺基质淋巴细胞生成素(thymic stromal lymphopoietin, TSLP)和趋化因子 CCL2 对人绒毛膜滋养细胞株 HTR-8/SVneo 中 IL-24 表达的影响; MTT 法分析重组 IL-24 和 CCL2 对 HTR-8/SVneo 细胞活力的影响。结果 IL-24 及其受体均在正常早孕期绒毛组织滋养细胞中强阳性表达。与对照组相比, 重组 CCL2 体外刺激后 HTR-8/SVneo 细胞 IL-24 表达水平显著下降(P<0.001)。重组 IL-24 处理后, HTR-8/SVneo 细胞活力显著降低(P<0.05 或 P<0.001); 相反, IL-24 中和性抗体明显促进其细胞活力(P<0.05 或 P<0.01), 重组 CCL2(100 ng/mL)可体外增强 HTR-8/SVneo 细胞活力(P<0.01), 但这一作用可被重组 IL-24 所抑制。结论 CCL2 通过抑制 IL-24 分泌增强人滋养细胞株 HTR-8/SVneo 细胞的体外活力, 从而可能有利于胚胎植入和胎盘发育。

【关键词】 白细胞介素-24(IL-24); CCL2; 滋养细胞; HTR-8/SVneo 细胞; 细胞活力

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CCL2 enhances the viability of human trophoblast cell line HTR-8/SVneo cells by inhibiting interleukin-24 expression

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Abstract
Objective To investigate the effect of interleukin-24 (IL-24) on the viability of human trophoblast cells. Methods Immunohistochemistry was used to detect the expression of IL-24 and its receptors (IL-20R1, IL-20R2 and IL-22R1) in villi from women with normal pregnancy. In-cell Western was performed to analyze the effects of recombinant thymic stromal lymphopoietin (TSLP) and chemokine CCL2 on the secretion of IL-24 by human chorionic trophoblast cell line HTR-8/SVneo cells. MTT assay was used to investigate the effects of recombinant IL-24 and CCL2 proteins on the viability HTR-8/SVneo cells in vitro.
Results IL-24 and its receptors were strong positively expressed in trophoblast cells of villi from women with normal pregnancy. Compared with control group, the expression of IL-24 in HTR-8/SVneo cells was significantly decreased after stimulation with recombinant CCL2 ($P<0.001$). Treatment with recombinant IL-24 significantly decreased the viability of HTR-8/SVneo cells ($P<0.05$ or $P<0.001$); on the contrary, IL-24 neutralizing antibody significantly enhanced the viability of HTR-8/SVneo cells ($P<0.05$ or $P<0.01$). In addition, recombinant CCL2 (100 ng/mL) enhanced the viability of HTR-8/SVneo cells ($P<0.01$) in vitro, but this effect could be inhibited by recombinant CCL24. Conclusion CCL2 enhances the viability of human trophoblast cell line HTR-8/SVneo cells in vitro by inhibiting the secretion of IL-24, which may be beneficial to blastocyst implantation and placental development.

Key words Interleukin (IL)-24; CCL2; Trophoblasts; HTR-8/SVneo cells; Cell viability

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卵巢子宫内膜异位囊肿取卵术后并发盆腔脓肿和肠梗阻：
病例分析1例并文献复习

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【摘要】目的：探讨子宫内膜异位症(EMS)不孕患者助孕策略的选择。卵巢子宫内膜异位囊肿保守治疗
的风险及取卵术后并发盆腔脓肿的风险与预防。方法：分析1例通过卵巢子宫内膜异位囊肿取卵术后并发
盆腔脓肿和肠梗阻病例并文献复习。结果：EMS不孕患者取卵后并发盆腔脓肿、盆腔粘连及部分小肠
梗阻保守治疗失败后行手术治疗。结论：EMS不孕症综合年龄、卵巢功能、疾病严重程度及男方因素等
选择最佳的助孕策略。为预防EMS取卵后感染的发生，在取卵术前要进行更彻底的阴道准备，术中规范操作
避免反复穿刺阴道壁，同时避免穿刺巧克力囊肿，术后广谱抗生素预防感染。对于已合并盆腔感染患者，
考虑将胚胎冷冻后择期移植。

【关键词】 卵巢子宫内膜异位囊肿; 盆腔脓肿; 肠梗阻; 取卵术; 体外受精-胚胎移植(IVF-ET)

【基金项目】国家自然科学基金项目(81300546)
Ovarian endometriosis cyst concurrent with pelvic abscess and intestinal obstruction after oocyte retrieval: 1 case analysis and literature review  
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【Abstract】Objective  To investigate the reproduction strategy choice of endometriosis (EMS) patients with infertility, the risk of ovarian EMS cyst treated conservatively, the risk and prevention of ovarian EMS cyst concurrent with pelvic abscess after oocyte retrieval.  
Methods  A case about ovarian endometriosis cyst concurrent with pelvic abscess and intestinal obstruction after oocyte retrieval was analyzed and the literatures were reviewed.  
Results  The EMS infertile patient complicated with pelvic abscess, basin celiac adhesion and part of intestinal obstruction after oocyte retrieval failed in conservative treatment and was finally cured with surgery.  
Conclusion  To select the best assisted reproduction strategy of EMS infertility, many factors should be considered comprehensively such as age, ovarian function, disease severity, and male factors. To prevent infection after oocyte retrieval, preoperative vaginal preparation could conduct more thorough before transvaginal oocyte retrieval, intraoperative standardized operation is contributed to avoid puncturing vaginal wall repetitively, at the same time avoid piercing chocolate cyst and use broad-spectrum antibiotics to prevent infection postoperatively. For patients with pelvic infection, frozen embryo and selective transfer are considered.  
【Key words】Ovarian endometriosis cyst; Pelvic abscess; Intestinal obstruction; Oocyte retrieval; In vitro fertilization-embryo transfer (IVF-ET)  
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新一代测序技术确诊1例遗传多囊肾病家系

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【摘要】目的 明确1例肝肾发育异常患儿的遗传学病因。方法 收集该患儿的家族史及临床资
料, 抽取患儿及其父母外周静脉血2mL, 对患儿基因组DNA进行新一代测序分析, 并对疑似致病性突
变位点进行Sanger测序验证及生物信息学预测。结果 该患儿系第三胎第一产, 前2胎均在围产期死
亡。B超示多囊肾表现。该患儿为男性, 4月大, 腹部膨隆可触及质硬包块。腹部超声提示多囊肾并肝
纤维化。新一代测序显示患儿PKHD1基因第30外显子c.3500T>C(p.L1167P)杂合突变, 遗传自母亲; 另
外患儿PKHD1基因第58外显子c.9235_9236delGCinsAA(p.A3079K)杂合突变, 来自父亲; 父母表型
均正常, 这2个突变均为新发现的突变。结论 该患儿是由PKHD1基因的复合杂合突变导致的常染色
体隐性遗传多囊肾病(ARPKD)。结合家族史推断, 该家系前2胎可能同样患有ARPKD。新一代测序
可对该类疾病明确诊断, 并有助于遗传咨询, 以避免该类悲剧的再次发生。

【关键词】常染色体隐性遗传多囊肾病(ARPKD); PKHD1; 新一代测序
Next generation sequencing for diagnosis of a patient with autosomal recessive polycystic kidney disease  
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【Abstract】Objective To investigate the genetic causes of a patient with liver and kidney dysplasia. Methods Clinical data of the patient and the family history were collected. The DNA of the patient and his parents was extracted and sequenced by next generation sequencing. The results were predicted and validated using Sanger sequencing.  
Results The patient was the first child and the third fetus in the family. The previous two fetuses were dead in the prenatal period with ultrasound showing polycystic kidney. The patient, a 4-month-old boy, had an abdominal distension with a touchable hard lump in his abdomen. Abdominal ultrasound revealed that he had polycystic kidney and fibrotic liver. Sequencing result showed a mutation of c.3500T>C (p.L1167P) in PKHD1 exon 30 inherited from his mother and a mutation of c.9235_9236delGCinsAA (p.A3079K) in PKHD1 exon 58 inherited from his father. Both mutations were novel mutations. Conclusion The patient was diagnosed as an autosomal recessive polycystic kidney disease (ARPKD) caused by PKHD1 compound heterozygous mutations. It is inferred that the previous two dead fetuses might suffer from ARPKD like this patient, thus the next generation sequencing contributes to diagnose such diseases and facilitates genetic counseling in order to avoid the family tragedy.  

【Key words】Autosomal recessive polycystic kidney disease (ARPKD); PKHD1; Next generation sequencing
现场调查

辅助生殖技术助孕患者健康信息需求现状及其影响因素分析

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【摘要】目的 了解和评估辅助生殖技术(assisted reproductive technology, ART)助孕患者的健康信息需求现状，并分析其影响因素。方法 采用一般资料调查表及 ART 助孕患者健康信息需求量表, 采用便利抽样法对南阳市中心医院、南阳市第一人民医院和南阳市医专一附院生殖门诊就诊的 622 例 ART 助孕患者进行信息需求现状调查。结果 ART 助孕患者信息需求总分为(114.87 ± 17.42)分, ART 助孕患者生育状态、年龄、不孕年限以及文化程度进入信息需求回归方程, 能够解释总变异的 49.3%。结论 ART 助孕患者信息需求水平较高, 是否生育、年龄、不孕年限以及文化程度是影响信息需求的重要因素, 医务人员应就其可控影响因素制定具有针对性的信息支持策略, 以提高医患信息交流满意度。

【关键词】 辅助生殖技术(ART); 信息需求; 影响因素分析
Current status and influencing factors of health information needs in patients undergoing assisted reproductive technology
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【Abstract】Objective  To investigate health information needs of patients undergoing assisted reproductive technology (ART), and analyze its influencing factors. Methods  A total of 622 patients undergoing ART were selected to fill in questionnaires including general information questionnaire and ART-Health Information Needs. Results  The overall information needs score for patients was 114.87 ± 17.42. Procreate or not, age, infertile duration, educational level and uterine condition entered the multiple regression equation and explained variance of 53.8%. Conclusion  Patients undergoing ART have higher information needs. Procreate or not, age, infertile duration and educational level are influencing factors of information needs.

【Key words】 Assistant reproductive technology (ART); Information needs; Influencing factors
推动卵子冷冻技术临床应用的若干思考

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【摘要】目的 分析卵子冷冻技术在我国的社会需求、临床应用的可行性及可能给管理带来的主要问题，提出政策建议。方法 检索国内外卵子冷冻技术相关文献，梳理国内外辅助生殖技术(ART)管理相关政策。结果 利用成熟的冷冻卵子进行体外受精-胚胎移植(IVF-ET)治疗的效果与新鲜卵子接近。我国卵子冷冻技术主要应用于取卵日男方取精失败的应急性冷冻卵子。卵子冷冻技术的短期风险较低，其应用具有临床意义和社会意义。社会因素卵子冷冻技术的伦理争议较多，但是存在一定的需求。结论 适时启动卵子冷冻技术临床应用的相关政策研究。审慎开展临床试点，科学进行舆论引导，不断加强技术评估。

【关键词】 卵子冷冻; 社会因素卵子冷冻; 管理; 政策建议
Perspectives about promoting the application of the oocyte cryopreservation  

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【Abstract】Objective To analyze the feasibility and necessity of the application of oocyte cryopreservation technology in China, and to give some suggestions to the management. Methods Domestic and international literatures on oocyte cryopreservation technology were searched. Results In vitro fertilization (IVF) with vitrified oocytes achieved similar outcomes to IVF using fresh oocytes. In our country, the egg freezing technology is mainly applied to the patients whose husbands fail to provide sperm samples at the time of oocyte pickup. Part of the centers has achieved reasonable outcomes. The short-term risk of egg freezing technology is relatively low, and its application has clinical validity and social significance. Although there are many theoretical debates surrounding oocyte cryopreservation for non-medical reasons, there are real needs. Conclusion It is necessary to timely launch policy research on oocyte cryopreservation, carefully proceed clinical trial, scientifically guide public opinion and constantly strengthen the technical assessment.

【Key words】Oocyte cryopreservation; Non-medical reason; Management; Policy proposal
辅助生殖技术对子代印记基因影响的研究进展

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【摘要】辅助生殖技术 (assisted reproductive technology, ART) 是采用医学技术手段使不孕不育夫妇获得妊娠一系列技术的统称, 与自然妊娠相比, 在体内、体外环境等有所不同。配子及早期胚胎的发育受多种因素影响, 致使子代健康风险增加。目前普遍认为 ART 与配子及早期胚胎的印迹基因异常有关, 进而影响子代出生后远期健康。本文就 ART 对印迹基因的影响进行综述, 分别从配子、植入前胚胎、胎盘等方面进行论述, 总结了 ART 与印迹基因异常的关系。

【关键词】辅助生殖技术 (ART); 印记基因; 甲基化

【基金项目】国家自然科学基金-面上项目(81671463)
Impacts of assisted reproductive technology on genomic imprinting in filial generation  

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【Abstract】Using a range of medical techniques to make infertile couples get pregnancy is collectively called assisted reproductive technology (ART), which is dissimilar from natural pregnancy in many respects such as in vitro and in vivo environments. Gametes and early embryos suffer from iatrogenic stress, and will cause an increase in children health risks. Currently, it is widely believed that ART is related to the abnormal expression of imprinted genes, and then affects the health of offspring. This paper reviews the impacts of ART on genomic imprinting from three aspects such as the gametes, preimplantation embryo and the placenta, which summarizes the relationship between assisted reproduction technology and the abnormal imprinted genes.  

【Key words】Assisted reproductive technology (ART); Imprinted genes; Methylation  

Fund program: Surface Program of National Natural Science Foundation of China (81671463)
促性腺激素释放激素激动剂降调节方案对子宫内膜容受性
的研究进展

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【摘要】 辅助生殖技术(ART)中, 子宫内膜容受性(ER)是影响女性妊娠成功与否的重要因素。促性腺激
素释放激素激动剂(GnRHa)在控制性卵巢刺激(COS)过程中得到广泛应用。GnRHa一方面解决了单纯促排卵导
致的早发黄体生成素(LH)峰造成卵子质量下降、周期取消率高问题, 另一方面能够通过调控激素及生物活
性因子(如雌激素及其受体、整合素、转化生长因子等)的分泌、胞饮突的形成。HOXA10等基因的
表达影响ER。本文总结了GnRHa调调节ER的机制, 综述了不同的GnRHa降调节方案(GnRHa超长方案、GnRHa
长方案、GnRHa短方案、GnRHa超短方案)对ER的影响, 为临床上制定合理、科学的个体化GnRHa降调
节方案提供参考。

【关键词】 体外受精-胚胎移植(IVF-ET); GnRH 激动剂(GnRHa); 子宫内膜容受性(ER)
Studies on GnRH agonist down-regulation protocols in regulation of endometrium receptivity  

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【Abstract】 Endometrium receptivity (ER) is a vital factor that affects women pregnancy in assisted reproductive techniques (ART). Gonadotropin-releasing hormone agonist (GnRHa) has been widely used in controlled ovarian stimulation (COS). GnRHa can not only prevent the premature luteinizing hormone (LH) surge-related worse follicles and higher cancellation rate caused by ovarian stimulation, but also affect the endometrium receptivity by regulating the secretion of hormones and bioactive molecules, such as estrogen and progesterone and their receptor, integrins and transforming growth factor (TGF). Moreover, GnRHa can affect the endometrium receptivity by regulating the number of pinopodes and the expression of HOXA10 gene. In this review we summarized the mechanism of GnRHa in regulating endometrium receptivity briefly, and then reviewed different GnRHa down-regulation protocols (prolonged GnRHa protocol, long GnRHa protocol, short GnRHa protocol and ultra-short GnRHa protocol) in the regulation of endometrium receptivity, and finally help clinicists to design the rational and individual down-regulation protocol of GnRHa.  

【Key words】 In vitro fertilization-embryo transfer (IVF-ET); Gonadotropin-releasing hormone agonist (GnRHa); Endometrium receptivity (ER)
黄体期使用促性腺激素释放激素激动剂的效果评价

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【摘要】 由于控制性超促排卵(COH)过程中超剂量雌、孕激素的生成以及垂体降调节药物的使用，经常出现黄体功能不全。需要常规进行黄体支持，常见的黄体支持方案包括使用人绒毛膜促性激素(hCG)及补充孕激索等。在近五年，多项研究表明促性腺激素释放激素激动剂(GnRH-a)在黄体支持中有很多方面，可以改善临床结局。其主要机制尚不清楚，可能与刺激黄体分泌雌、孕激素，提高子宫内膜容性，提高胚胎发育潜能，促进滋养细胞分泌hCG 相关。GnRHa 进行黄体支持的机制及用法用量还有待进一步探究。

【关键词】 促性腺激素释放激素(GnRH): 促性腺激素释放激素激动剂(GnRH-a): 黄体支持
Current progress on gonadotropin-releasing hormone agonist for luteal phase support  

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【Abstract】Luteal-phase deficiency is a common problem resulting from supraphysiological steroid hormone levels together with the suppressed luteinizing hormone (LH) levels by both gonadotropin-releasing hormone agonist (GnRH-a) and gonadotropin-releasing hormone antagonist (GnRH-A) administration during controlled ovarian hyperstimulation (COH) cycles. Therefore, luteal phase support is a common practice in IVF treatment. Most of these regimens involve the administration of human chorionic gonadotropin (hCG), estradiol (E2) and progesterone (P). Some recent data, however, have suggested a beneficial effect of GnRH-a administered in the luteal phase on assisted reproductive technique (ART) outcomes. The exactly mechanisms of actions and the ideal dose, administration route, and time interval of GnRH-a administration in the luteal phase support remain largely undetermined.  

【Key words】Gonadotropin-releasing hormone (GnRH); Gonadotropin-releasing hormone agonist (GnRH-a); Luteal phase support
子宮内膜微刺激与宮腔内人工授精患者妊娠结局的新研究

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【摘要】 卵巢刺激与宫腔内人工授精(IUI)是世界范围内治疗不孕患者经常用到的基本助孕方案, 但其临床妊娠率相对较低。相关文献表明内膜微刺激通过提高內膜容受性改善不同原因反复移植失败患者体外受精 - 胚胎移植(IVF-ET)的妊娠结局。这是否同样有益于改善 IUI 的妊娠结局呢？本文就有关内膜微刺激改善子宫内膜容受性的最新作用机制及 IUI 临床妊娠率能否得到改善的最新研究进行概述。

【关键词】 内膜微刺激; 宫腔内人工授精(IUI); 子宫内膜容受性; 临床妊娠率
Influence of endometrial mechanical stimulation on clinical pregnancy rate of intrauterine insemination

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【Abstract】The first line of fertility treatment frequently applied in the world is intrauterine insemination (IUI) with ovarian stimulation. The effectiveness of this procedure is, however, still low. There is evidence of significant difference on the clinical pregnancy rate when endometrial scratching performed prior to embryo transfer in women undergoing in vitro fertilization-embryo transfer (IVF-ET), who stand with repeated transfer failure. Is it also beneficial to IUI? Here, we present an overview about the up to date mechanism and the role of endometrial injury in the cycle preceding ovarian stimulation for IUI cycle on the clinical pregnancy rate.

【Key words】Endometrial scratch; Endometrial local injury; Intrauterine insemination (IUI); Endometrial receptivity; Clinical pregnancy rate
维生素 D 与男性不育关系的研究进展

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【摘要】维生素 D (vitamin D, VD) 作为一类常见的营养元素，不仅在调节钙稳态和骨骼健康方面具有明确的作用，近年来有研究发现其与男性生殖可能存在密切关系。本文通过阐述VD的代谢、VD与男性性激素、精子质量以及妊娠结局的关系，为进一步说明VD对男性生育力的重要影响，了解VD对男性生殖的影响及其机制可为临床诊疗提供新的思路和方法。

【关键词】 维生素 D (VD); 男性生殖; 性激素; 精子

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Vitamin D and male infertility: advances in studies  
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【Abstract】Vitamin D (VD) has a definite effect on the regulation of calcium homeostasis and bone health. As the research progresses, the relationship between VD and male reproduction has been gradually revealed. This article describes the important effects of VD on male fertility by expounding the relationship between VD metabolism, VD and male sex hormones, sperm quality and pregnancy outcomes. Understanding the effect of VD on male reproduction and its mechanism will provide new ideas and methods to the clinical diagnosis and treatment of male infertility.  

【Key words】Vitamin D (VD); Male reproduction; Sex hormones; Sperm  
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