

• 专家风采 •

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作为国家杰出青年基金获得者、科技部“生殖与发育大专项”首席科学家、教育部长江学者特聘教授、何梁何利奖获得者、吴阶平-保罗·杨森医学药学奖(吴杨奖)和首都百名科技领军人才, 一直从事妇产科及生殖健康相关的临床与基础研究工作, 在应用辅助生殖技术(试管婴儿)帮助数万名不孕患者得到有效治疗的同时, 从配子、受精、胚胎和着床等多方面进行系统深入的研究, 获国家科技进步二等奖二项、教育部科技进步奖一等奖及一项何梁何利科学与技术进步奖; 率领团队入选“教育部创新团队”、“教育部重点实验室”和“北京市重点实验室”。曾作为访问学者在香港大学学习, 并在美国斯坦福大学做博士后研究。2013年与北大合作完成了对人单个卵母细胞的高精度全基因组测序, 成果发表在国际著名学术期刊《Cell》杂志上。

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• 实验研究 •

米非司酮通过调节岩藻糖基转移酶 IV 的表达抑制胚胎体外黏附

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【摘要】目的: 探讨米非司酮对人胚胎细胞 JAR 与人子宫内膜细胞 RL95-2 之间黏附的影响及其调控的分子机制。方法: 采用黏附实验分别观察 RU486 以及岩藻糖基转移酶 IV(FUT4) 对 JAR 细胞与 RL95-2 细胞之间黏附的影响。采用 RT-PCR 以及 Western blotting 检测米非司酮对 RL95-2 细胞以及流产妇女子宫内膜中 FUT4 表达的调控。结果: ①米非司酮抑制 JAR 细胞与 RL95-2 单层细胞之间的黏附; ②米非司酮抑制 RL95-2 细胞以及流产妇女子宫内膜中 FUT4 基因和蛋白的表达; ③ FUT4 质粒转染 RL95-2 细胞后, 调节 JAR 细胞与 RL95-2 单层细胞之间的黏附。结论: 米非司酮通过调节 FUT4 的表达抑制胚胎体外黏附。

关键词: 米非司酮; 岩藻糖基转移酶 IV(FUT4); 子宫内膜; 黏附

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Mifepristone Inhibits the Adhesion of Embryos *in vitro* by Decreasing the Expression of Fucosyltransferase IV

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【ABSTRACT】Objective: To investigate the effect of mifepristone on the adhesion of JAR cells to RL95-2 cells monolayer and its regulation mechanism. **Methods:** The adhesion of JAR cells to RL95-2 cells monolayer which was treated with mifepristone or fucosyltransferase IV (FUT4) plasmid was detected by cell counting. The regulation of mifepristone via FUT4 in RL95-2 cells and in human endometrial tissues was examined by RT-PCR and Western blotting. **Results:** 1) Mifepristone inhibited the adhesion of JAR cells to RL95-2 cells monolayer. 2) Mifepristone inhibited the expression of FUT4 in RL95-2 cells and in human endometrial tissues by RT-PCR and Western blotting. 3) The adhesion of JAR cells to RL95-2 cell monolayer was inhibited by FUT4-siRNA. Inversely, the percent of adhesion was promoted by FUT4 over-expression plasmid. **Conclusion:** Mifepristone inhibits the adhesion of embryos *in vitro* by decreasing the expression of FUT4.

Key words: mifepristone; fucosyltransferase IV (FUT4); endometrium; adhesion

人子宫内膜细胞体外诱导蜕膜化的效果观察

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【摘要】目的: 观察孕激素(progesterone, P)、雌激素(estrogen, E₂)和8-溴-环磷酸腺苷(8-Br-cAMP)不同组合的3种方法对人子宫内膜细胞体外诱导蜕膜化的效果。方法: 收集因子宫良性病变行全子宫切除术患者的子宫内膜, 分离纯化子宫内膜间质细胞(endometrial stromal cell, ESC), 进行细胞体外培养并传代, 免疫荧光鉴定细胞类型。分别采用P+E₂(PE组)、8-Br-cAMP(PC组)、P+E₂+8-Br-cAMP(PEC组)3种不同组合方法蜕膜化诱导处理第3代ESC, 并以空白对照为对照组。显微镜下观察蜕膜化过程中的细胞形态变化, 化学发光法检测3种不同蜕膜化诱导方法处理24 h、48 h及96 h后细胞培养液中催乳素(PRL)水平, 比较3种蜕膜化方法的效果。结果: 蜕膜化过程中ESC形态从长梭形逐渐变为圆形, 细胞体积变大, 胞核增大, 部分出现双核或多核, 细胞边界变模糊。随着培养时间延长, 各蜕膜化诱导组培养液中PRL呈不同水平升高。其中PC组PRL水平及蜕膜化细胞形态均较PE组和PEC组升高明显($P < 0.05$)。结论: P+8-Br-cAMP法, 较P+E₂、P+E₂+8-Br-cAMP法能更有效地诱导子宫ESC体外发生蜕膜化, 是高效可靠、更合适的蜕膜化诱导方法。

关键词: 子宫内膜细胞; 蜕膜化; 8-溴-环磷酸腺苷(8-Br-cAMP); 雌激素(E₂); 孕激素(P)

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Comparison of Three Methods on Decidualization of Human Endometrial Cells *in Vitro*

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【ABSTRACT】 Objective: To observe the effect of three different methods on decidualization of human endometrial cells *in vitro*. **Methods:** Human endometrial tissues were obtained from women undergoing hysterectomies for uterine benign diseases. Endometrium stromal cells (ESCs) were separated and cultured *in vitro* and identified by immunofluorescence. The 3rd generation of ESCs were treated with progesterone (P) + estrogen (E₂)(PE group), P+8-Br-cAMP (PC group) and P+E₂+8-Br-cAMP (PEC group), respectively. The cell morphology was observed under the microscope, and the PRL level of cell-culture medium in 24 h, 48 h and 96 h were detected using chemiluminescence method. **Results:** ESCs became round with bigger cell volume and nucleus, and the cell boundaries became ambiguous during decidualization. Among these three different groups, cells treated with P+8-Br-cAMP showed more obvious changes in both PRL level and cell morphology. **Conclusion:** Compared with P+E₂ and P+E₂+8-Br-cAMP, P+8-Br-cAMP is a more effective method on induction of decidualization of endometrial cells *in vitro*.

Key words: endometrial cell; decidualization; 8-Br-cAMP; estrogen (E₂); progesterone (P)

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胶原酶分离及低速离心结合筛网过滤法 纯化子宫内膜细胞的研究

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【摘要】目的: 探索分离子宫内膜细胞以及纯化子宫内膜腺上皮细胞与间质细胞的最好方法。方法: 采用 I 型胶原酶、胰酶、I 型胶原酶混合胰酶以及机械研磨等 4 种方法处理大鼠子宫, 比较细胞数和活细胞率, 从而获得分离子宫内膜组织的最好方法。用获得的最好方法分离人类子宫内膜组织, 比较采用 2 次筛网过滤(筛网法)和低速离心结合筛网过滤(结合法)进一步纯化子宫内膜腺上皮细胞和间质细胞获得的细胞数和纯化效率, 从而获得较好的纯化方法。结果: I 型胶原酶、胰酶、I 型胶原酶混合胰酶和机械研磨处理大鼠子宫组织所得的细胞数分别为 $6.43 \pm 3.55 \times 10^5/\text{ml}$ 、 $4.59 \pm 2.35 \times 10^5/\text{ml}$ 、 $4.25 \pm 1.06 \times 10^5/\text{ml}$ 、 $3.57 \pm 1.15 \times 10^5/\text{ml}$, 差异有统计 * \bar{x} ($P < 0.05$); 活细胞率分别为 $98.90 \pm 0.74\%$ 、 $96.63 \pm 1.84\%$ 、 $97.97 \pm 2.02\%$ 、 $97.20 \pm 4.41\%$, 差异无统计学意义($P > 0.05$)。筛网法和结合法纯化分离所获得的腺上皮细胞数为 $0.43 \pm 0.21 \times 10^5/\text{ml}$ 、 $8.27 \pm 2.46 \times 10^5/\text{ml}$; 间质细胞纯度为 $92.94 \pm 2.89\%$ 和 $99.19 \pm 0.24\%$, 差异均有统计学意义($P < 0.05$)。结论: I 型胶原酶是分离子宫内膜细胞的最好方法, 而采用低速离心结合筛网过滤法是较理想的纯化分离后的子宫内膜细胞的方法。

关键词: 腺上皮细胞; 间质细胞; I 型胶原酶; 低速离心; 筛网过滤

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Separating and Purifying Endometrial Cells Using Collagenase I and Low-speed Centrifugation Combined with Screen Filter

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【ABSTRACT】Objective: To explore an optimal method of separating and purifying endometrial glandular epithelial cells and stromal cells. **Methods:** Using four methods (collagenase I + DNase, trypsin + DNase, collagenase I + trypsin + DNase and mechanical grinding + DNase) to separate rat uterine cells, the best method was obtained by comparing the cell count and live-cell rate. Then human endometrial cells were separated by the best method, then purified by the following two methods: 1) twice screen filtering (screen filter method), 2) low-speed centrifugation combined with screen filtering (combined method). The better method was obtained by comparing the cell count and cell purity. **Results:** The cell counts of the rat uterus digested by collagenase I + DNase, trypsin + DNase, collagenase I + trypsin + DNase and mechanical grinding + DNase were $6.43 \pm 3.55 \times 10^5/\text{ml}$, $4.59 \pm 2.35 \times 10^5/\text{ml}$, $4.25 \pm 1.06 \times 10^5/\text{ml}$, $3.57 \pm 1.15 \times 10^5/\text{ml}$, respectively, there was a significant difference ($P < 0.05$), but no significant difference ($P > 0.05$) was found in the live-cell rates, which were $98.90 \pm 0.74\%$, $96.63 \pm 1.84\%$, $97.97 \pm 2.02\%$, $97.20 \pm 4.41\%$, respectively. As for screen filter method and combined method, the cell count of granular epithelial cells were $0.43 \pm 0.21 \times 10^5/\text{ml}$ and $8.27 \pm 2.46 \times 10^5/\text{ml}$; the cell purity of stromal cells were $92.94 \pm 2.89\%$ and $99.19 \pm 0.24\%$, showing a significant difference ($P < 0.05$). **Conclusion:** Collagenase I was the optimal method of separating endometrial cells, and the better method for purifying human endometrial granular epithelial cells and stromal cells was low-speed centrifugation combined with screen filtering.

Key words: glandular epithelial cells; stromal cells; collagenase I ; low-speed centrifugation; screen filtering

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• 临床研究 •

低剂量重组人促卵泡刺激素(rFSH)递增方案 诱导排卵的多中心前瞻性研究

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【摘要】目的: 探讨在低剂量重组人促卵泡刺激素(rFSH)递增方案诱导排卵中临床结局的预测因子。方法: 总结全国22家生殖中心对WHO II型无排卵为主要不孕原因的患者使用低剂量rFSH递增方案共433个诱导排卵周期中418个符合疗效分析的周期的临床妊娠率、单卵泡发生率、周期取消率、卵巢过度刺激综合征(OHSS)发生率; 比较37.5 IU和75.0 IU不同rFSH启动剂量的临床、实验室结局, 分析单卵泡发育、卵巢诱导成功、周期取消与年龄、体质量指数(BMI)、卵巢储备等预测因子间的关系。结果: ①所有对象临床妊娠率为17.94%, 单卵泡发育率为57.66%, OHSS发生率为2.31%, 多胎妊娠率为0.23%, 周期取消率为12.68%; ②果纳芬(rFSH)平均治疗天数为 12.7 ± 5.6 d, 平均总使用剂量为 813.8 ± 480.4 IU, 平均阈剂量为 73.0 ± 29.7 IU; 其中75.12%的患者总使用剂量 $<1\ 000$ IU, 73.68%的人群刺激天数在5~15 d之间; ③启动剂量为37.5 IU者较启动剂量为75 IU者的卵巢诱导时间明显增加(14.1 ± 5.6 d vs 10.9 ± 4.9 d, $P=0.000$), 果纳芬总使用剂量明显减少(767.0 ± 495.0 IU vs 879.1 ± 542.7 IU, $P=0.000$), 单卵泡发育率明显增加(62.30% vs 51.15% , $P=0.027$), 周期取消率明显升高(17.62% vs 5.75% , $P=0.000$); OHSS发生率无明显差异(2.87% vs 1.72% , $P=0.532$), 临床妊娠率和生化妊娠率亦无统计学差异($P>0.05$); ④不同阈剂量下临床妊娠率和生化妊娠率均无统计学差异($P>0.05$); 体质量 ≥ 70 kg时阈剂量明显增加; ⑤周期取消的预测因素与年龄呈负相关($r=-0.169$, $OR=0.845$, $95\%CI=0.744\sim 0.960$, $P=0.010$), 与既往诱导排卵周期数呈正相关($r=0.240$, $OR=1.271$, $95\%CI=1.093\sim 1.478$, $P=0.002$)。结论: 低剂量递增方案诱导排卵可以取得较高的单卵泡发育率和临床妊娠率, 且降低并发症发生率。不同启动剂量与刺激天数和总使用剂量相关, 但对临床结局无明显影响; 周期取消可能与年龄和既往诱导排卵周期有关。

关键词: 低剂量; 重组人促卵泡刺激素(rFSH); 递增方案; 单卵泡发育; 卵巢反应预测因子

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Factors Related to Successful Ovulation Induction with Low-dose Recombinant FSH Treatment

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【ABSTRACT】 Objective: To investigate the predictive factors for clinical outcome in low-dose step-up recombinant follicle stimulating hormone (rFSH) protocol for ovulation induction. **Methods:** A total of 433 infertile parities, majority of them with WHO group II anovulatory infertility from 22 ART centers in China, underwent a low-dose step-up rFSH protocol for ovulation induction. The clinical pregnancy rate, mono-follicular development rate, cycle cancellation rate and OHSS rate were assessed in 418 cycles fitted with efficacy population. A comparison of difference in duration of ovulation induction, total gonadotrophin dose, mono-follicular development rate, achieve follicular development rate, clinical pregnancy rate and cycle cancellation rate between 37.5 IU and 75 IU starting dose was performed. Age, body mass index (BMI) and ovarian reserve considered as predictive factor were analyzed to investigate the correlation with mono-follicular development, achieve follicular development, and cycle cancellation. **Results:** 1) Of overall subjects, clinical pregnancy rate was 17.94%, mono-follicular development rate was 57.66%, OHSS rate was 2.31%, multiple pregnancy rate was 0.23% and cycle cancellation rate was 12.68%; 2) Mean duration of Gonal-f administration was 12.7 ± 5.6 d, mean total dose of Gonal-f (rFSH) was 813.8 ± 480.4 IU, mean threshold dose was 73.0 ± 29.7 IU. Total dose of Gonal-f was less than 1 000 IU in 75.12% of subjects and duration of stimulation was between 5–15 d in 73.68% of subjects. 3) Duration of ovulation induction was significantly longer in the 37.5 IU starting dose group than in the 75 IU group (14.1 ± 5.6 d vs 10.9 ± 4.9 d, $P=0.000$). Total dose of Gonal-f was significantly decreased in 37.5 IU group compared with the 75 IU group (767.0 ± 495.0 IU vs 879.1 ± 542.7 IU, $P=0.000$). A significantly increase in the mono-follicular development rate was observed in the 37.5 IU group than in the 75 IU group (62.30% vs 51.15%, $P=0.027$). There was no statistically significant difference in terms of clinical pregnancy rate and biochemical pregnancy rate ($P>0.05$), but cycle cancellation rate was significantly higher in 37.5 IU group than in the 75 IU group (17.62% vs 5.75%, $P=0.000$). OHSS rate was not significantly different between 37.5 IU group and 75 IU group (2.87% vs 1.72%, $P=0.532$). 4) There were no statistically significant differences in terms of clinical pregnancy rate and biochemical pregnancy rate according to different threshold doses ($P>0.05$). A significant increase in the threshold dose was observed when body weight was more than 70 kg. 5) Age was negatively correlated with cycle cancellation ($r=-0.169$, $OR=0.845$, 95%CI=0.744–0.960, $P=0.010$) and the number of ovulation induction treatment cycles was a positive predictive factor for cycle cancellation ($r=-0.240$,

$OR=1.271$, 95% $CI=1.093-1.478$, $P=0.002$). **Conclusion:** A low-dose step-up rFSH protocol may result in not only high mono-follicular development rate and clinical pregnancy rate but also a significant decrease in the incidence of OHSS. Different starting doses may lead to different duration of ovulation induction and total gonadotrophin without affecting clinical outcomes. The influence of cycle cancellation seems to be age and the number of ovulation induction treatment cycles.

Key words: low-dose step-up protocol; mono-follicular development; prediction model

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IVF/ICSI-ET技术中单卵双胎的发生及其相关因素

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【摘要】 目的: 探讨潜在的可能导致体外授精/卵胞质内单精子注射-胚胎移植(IVF/ICSI-ET)技术单卵双胎(MZT)高发生率的因素及其可能机制。方法: 回顾性分析行IVF/ICSI-ET的2 885个周期, 其中新鲜胚胎移植2 184个周期(常规IVF-ET周期1 473个, ICSI周期711个)和冻融胚胎移植(FET)周期701个, 统计各个周期MZT妊娠的发生率, 并分析可能影响其发生的相关因素。结果: 在2 885个周期中临床妊娠1 102例, 多胎妊娠的发生率为20.78%(229/1 102), 其中MZT(双绒毛膜双胎及单绒毛膜双胎)妊娠20例, 占临床妊娠的1.81%(20/1 102), 占多胎的8.73%(20/229)。MZT中单卵双绒毛膜双胎5例, 占MZT的25%(5/20), 单卵单绒毛膜双胎15例, 占MZT的75%(15/20)。ICSI中MZT的发生率为1.76%(5/284), 高于常规IVF-ET周期(1.56%, 9/575), 但无统计学差异($P>0.05$)。FET组701个周期中临床妊娠243个周期, 多胎34例, MZT 6例, 占多胎发生率的17.65%(6/34); 新鲜移植的2 184个周期中临床妊娠859个周期, 多胎195例, MZT 14个周期, 占多胎发生的7.18%(14/195), FET组和新鲜周期移植组间多胎率有统计学差异($P<0.05$)。囊胚移植204个周期中妊娠95例, 多胎12例, MZT 3例, 占多胎发生的25%(3/12), 非囊胚移植2 681个周期中妊娠1 007例, 多胎217例, MZT 17例, 占多胎发生的7.83%(17/217), 囊胚移植组与非囊胚移植组间多胎率有统计学差异($P<0.05$)。冻融囊胚移植发生MZT的几率显著高于冻融非囊胚移植($P<0.05$)。IVF-ET中MZT妊娠与非MZT妊娠患者的年龄、促排卵方案、促排卵天数、促性腺激素(Gn)剂量与时间、优质胚胎数、移植胚胎数之间均无统计学差异($P>0.05$)。结论: MZT的发生率IVF/ICSI-ET明显高于自然妊娠; 冻融囊胚移植明显高于冻融非囊胚移植, 这可能与体外培养条件和冷冻复苏技术的应用有关, 使其透明带硬度有所增加, 致使囊胚在孵出时较易嵌顿, 从而导致了MZT的发生。单纯显微授精技术不会明显增加MZT的发生率。

关键词: 单卵双胎(MZT); 体外受精/卵胞质内单精子注射-胚胎移植(IVF/ICSI-ET); 冻融胚胎移植(FET); 囊胚移植

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Incidence and Related Factors Analysis of Monozygotic Twinning in IVF/ICSI-ET

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【ABSTRACT】 Objective: To investigate the monozygotic twinning (MZT) pregnancy occurred in *in vitro* fertilization/ intracytoplasmic sperm injection-embryo transfer (IVF/ICSI-ET) and analyze the potential possible factors which may lead to high incidence of MZT in IVF/ICSI-ET. **Methods:** A retrospective study was performed on women with MZT pregnancy in 1 473 conventional IVF-ET cycles, in 711 ICSI cycles and in 701 frozen-thawed embryo transfer (FET) cycles. The incidence rate of MZT in IVF/ICSI-ETs was investigated, and relevant factors that may affect its occurrence were analyzed. **Results:** The number of gestational sac which was greater than the number of embryos transferred (double-chorionic twins) or a single gestation with the intracapsular two germs and heart tube pulsation (monochorionic twins) were diagnosed as MZT. There were 1 102 clinical pregnancies of 2 885 IVF/ICSI-ET cycles in our center, the multiple pregnancy rate was 20.78%, of which 20 cases of MZT pregnancies, accounting for 1.81% of clinical pregnancies, accounting for 8.37% of multiple births. Five cases of MZT were monozygotic pairs chorionic twins, accounting for 25% of the MZT, 15 cases were monozygotic MZT, accounting for 75% of the MZT. The incidence rate of MZT between conventional IVF-ET cycles and ICSI cycles was not significantly different. There were 243 clinical pregnancies of FET, 34 cases multiple births, 6 cases of MZT, accounting for 17.65% of the incidence of multiple births. There were 859 clinical pregnancies in the transplantation of the fresh cycles, 195 cases of multiple births, 14 cases of MZT, multiple births occurred in 7.18%. There were significant differences between routine IVF group and ICSI group ($P<0.05$). Among 204 cycles of blastocyst transfer, 95 cases were pregnant, 12 cases of multiple births, 3 cases of MZT, accounting for 25% of multiple births, among 1 007 pregnancy cases in non-blastocyst transfer, 217 cases of multiple births, 17 cases of MZT, accounting for 7.83% of the occurrence of multiple births in both groups, with a significant difference ($P<0.05$). Compared with the probability of occurrence of MZT was significantly higher in frozen-thawed blastocyst transfer than in frozen-thawed non-blastocyst transfer ($P<0.05$). There were no significant differences between MZT and the age of ovulation induction, ovulation days, the dose and the duration of gonadotropin (Gn) and the number of embryos ($P>0.05$). **Conclusion:** The incidence rate of MZTs in IVF/ICSI-ET cycles was significantly higher than that in natural pregnancy. This may be related to the application of *in vitro* culture conditions and cryopreservation techniques. Blastocyst transfer in FET transfer can be significantly increased incidence of MZT, may be the embryos cultured *in vitro* time, making it the zona pellucida hardness has increased, resulting in blastocyst hatching easier incarcerated, resulting in the occurrence of MZT. Simple microscopic insemination technology and frozen-thawed procedure will not significantly increase the incidence of MZT.

Key words: monozygotic twinning (MZT); *in vitro* fertilization-embryo transfer/intracytoplasmic sperm injection (IVF/ICSI-ET); frozen-thawed embryo transfer (FET); blastocyst transfer

多囊卵巢综合征患者子宫内膜不典型增生的药物转化分析

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【摘要】 目的: 分析多囊卵巢综合征(PCOS)患者子宫内膜不典型增生的药物转化疗效及安全性。方法: 回顾性分析17例PCOS子宫内膜不典型增生患者, 其中9例曾用孕激素治疗未转化者为A组; 8例未曾治疗者为B组, 均检测口服葡萄糖耐量试验(OGTT)并同时行胰岛素释放试验, 以检测患者是否存在胰岛素抵抗(IR)及高胰岛素血症。17例患者均采用口服避孕药联合二甲双胍治疗。结果: 17例PCOS患者均存在IR及高胰岛素血症, 经药物治疗3~6个周期后, 内膜不典型病变均成功转化。结论: 采用口服避孕药联合二甲双胍治疗PCOS合并IR的子宫内膜不典型增生患者是一种临床上实用、有效的治疗方法。

关键词: 多囊卵巢综合征(PCOS); 子宫内膜不典型增生; 胰岛素抵抗(IR); 口服避孕药(OC); 二甲双胍

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Drug Transformation Analysis of Endometrial Atypical Hyperplasia in Patients with Polycystic Ovary Syndrome (PCOS)

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【ABSTRACT】 Objective: To analyze the efficacy and safety of drugs on reverse of atypical endometrial hyperplasia in patients with polycystic ovary syndrome (PCOS). **Methods:** A retrospective analysis on 17 patients with PCOS complicated by atypical endometrial hyperplasia was performed (9 patients who were treated with progestin but not reversed were considered as group A; 8 patients who were untreated were considered as group B). Both groups received OGTT and insulin release test, to check whether the patients had insulin resistance (IR) or hyperinsulinemia. The 17 patients were treated with oral contraceptives combined with metformin. **Results:** After the 17 patients with PCOS complicated by IR and hyperinsulinemia received drug treatment for 3–6 cycles, atypical endometrial hyperplasia was successfully reversed. **Conclusion:** Oral contraceptives combined with metformin is a clinically practical and effective method for treatment of PCOS complicated by atypical IR endometrial hyperplasia.

Key words: polycystic ovary syndrome (PCOS); endometrial atypical hyperplasia; insulin resistance (IR); oral contraceptive pills (OC); metformin

• 流行病学研究 •

2 054例围绝经期及绝经后妇女宫内节育器 使用年限及取出情况调查

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【摘要】目的: 了解围绝经期及绝经后妇女宫内节育器(IUD)的取出情况及实际使用年限。方法: 以在黄浦区居住且末次使用避孕方法为IUD的45~60岁妇女为研究对象, 于2011.08~12期间开展横断面调查, 共调查2 167人, 其中2 054人纳入分析。结果: 研究对象平均年龄 52.4 ± 4.0 岁。1 160例已绝经的妇女中, 63例(5.4%)使用的IUD仍未取出, 其中15例IUD已放置至绝经后5年以上; IUD的平均宫内放置时间为 18.9 ± 5.7 年, 50.2%的IUD使用者宫内放置时间 >20 年。732例未绝经的妇女中, IUD的平均使用年限为 17.3 ± 5.7 年, 有51.1%的女性使用IUD已超出建议使用期限。结论: 绝经后IUD过期使用情况严重, 相当一部分正在使用的IUD已超过了使用期限。

关键词: 宫内节育器(IUD); 围绝经期; 使用期限; 取出率

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Removal Rate and Service Time of Intrauterine Devices among 2 054 Peri- or Postmenopausal Women

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【ABSTRACT】 Objective: To estimate the removal rate and the service time of intrauterine devices (IUDs) in uterine among peri- or post-menopausal women. **Methods:** A cross-sectional study was developed in Huangpu District, Shanghai between August and December 2011. A total of 2 167 women aged 45–60 years were interviewed who used IUD as the last contraceptives and lived in Huangpu District. Totally 2 054 women were included in final analysis. **Results:** The mean age of participants was 52.4 ± 4.0 years. Among 1 160 postmenopausal women, 63 (5.4%) had not removed the IUDs. The mean duration of service of IUDs in uterus was 18.9 ± 5.7 years, and 50.2% of IUDs had stayed in uterus for ≥ 20 years. Among 732 women before menopause, the mean service time of IUDs in uterus was 17.3 ± 5.7 years, and 51.1% of IUDs in use had exceeded the recommended service time. **Conclusion:** Most of the IUDs had been removed after menopause. However, quite a lot of IUDs in use had exceeded their recommended lifespans.

Key words: intrauterine device (IUD); peri-menopausal period; duration of placement; removal rate

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· 综述 ·

免疫抑制因子 MNSF β 在母-胎界面 作用机制的研究进展

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【摘要】 母-胎界面免疫耐受状态的形成是胚胎植入和妊娠维持过程中的一个关键环节, 唯其机制尚不十分清楚。单克隆非特异性抑制因子- β (MNSF β)(Fau)是一种在体内广泛分布的非抗原特异性的免疫抑制因子, 能抑制激活型 T 细胞和 B 细胞的增殖, 以及 T 细胞和巨噬细胞中 TNF α 等细胞因子的表达, 并在胚胎植入及妊娠维持过程中发挥重要作用。由文献报道推测: MNSF β 蛋白有分泌型和非分泌型2种表达形式, 而且前者是以完整的MNSF β 蛋白分子单体或多聚体形式分泌到细胞外, 后者以 MNSF β 蛋白的 Ubi-L 肽段分别与 Bcl-G 或 endophilin II 形成复合物的形式存在于细胞质中。MNSF β 对蜕膜巨噬细胞(dMac)中 Cox-2 和 p53 表达的抑制是不利于胚胎植入和妊娠维持的。

关键词: 母-胎界面; 单克隆非特异性抑制因子- β (MNSF β); 免疫耐受; 细胞因子

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Roles of MNSF β Played at the Maternal-fetal Interface

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【ABSTRACT】 The formation and maintaining of the immune tolerance at the maternal-fetal interface is the pivotal event during the embryo implantation and subsequent pregnancy process, but the mechanisms underlying this phenomenon are still not fully understood. Monoclonal nonspecific suppressor factor β (MNSF β) (Fau) is a ubiquitously distributed cytokin that possesses an antigen-nonspecific immune-suppressive function, and plays critical roles in embryo implantation and early pregnancy. The report from the literatures speculated that MNSF β protein was divided into two forms of expression: secreted and non-secreted protein. The former was secreted into the extracellular in the complete monomer or polymer form of MNSF β protein molecules and the latter existed in the cytoplasm in the forms of the Ubi-L peptide segments and Bcl-G or endophilin II complex. The inhibition of Cox-2 and p53 expression in the decidual macrophages (dMac) by MNSF β was not conducive to the maintenance of embryo implantation and pregnancy.

Key words: maternal-fetal interface; monoclonal nonspecific suppressor factor β (MNSF β); immune tolerance; cytokine

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子宫内膜容受性的表观遗传调控机制的研究进展

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【摘要】表观遗传在调控子宫内膜容受性和胚胎植入方面有重要作用。表观遗传学调控参与月经周期子宫内膜再生和增殖、血管形成、植入和蜕膜化。DNA甲基化与EMs发生有关, 卵巢癌相关的肿瘤抑制基因的高甲基化导致基因表达沉默, 很多与子宫内膜癌相关的肿瘤基因都有异常甲基化变化, 进而发生肿瘤。组蛋白修饰参与许多妇科疾病的发生过程, 其中部分妇科疾病正是因为改变子宫内膜容受状态进而导致不孕。组蛋白修饰和DNA甲基化之间也可以相互调控, 同时组蛋白乙酰化也可以调节DNA甲基化。缺少miRNA的表达与某些人类子宫内膜疾病相关, 例如EMs、子宫内膜增生和肿瘤, 这些疾病影响子宫内膜的厚度、血流状态、分子表达进而降低子宫内膜的容受性, 导致不孕。

关键词: 子宫内膜容受性; 表观遗传; DNA甲基化; 组蛋白修饰; microRNA (miRNA)

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Advances in Study on Mechanisms of Epigenetic Regulation Underlying Endometrial Receptivity

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【ABSTRACT】 Epigenetic regulation is very important to endometrial receptivity and embryo implantation. Epigenetic regulation is involved in the process of regeneration and proliferation of endometrium, angiogenesis, implantation and decidulization. DNA methylation acts on the development of EMs and hyper-methylation of some ovarian tumor suppressor genes leading to gene silencing, while the abnormal methylation has been found in many tumor related genes of endometrial cancer. Histone modification takes part in the process of the occurrence and development of many gynecological diseases, part of which will lead to infertility by changing the state of endometrial receptivity. Histone modification and DNA methylation can regulate each other, meanwhile histone acetylation may influence the process of DNA methylation. Some human endometrial diseases including EMs, endometrial hyperplasia and tumor, which will influence the thickness, blood flow and molecular expressions of endometrium, are related with the absence of some miRNA.

Key words: endometrial receptivity; epigenetic regulation; DNA methylation; histone modification; microRNA

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卵巢早衰的研究现状与进展

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【摘要】 卵巢早衰(POF)是生殖医学的一大难题, 卵子形成与发育的任一环节受损都有可能导致POF。POF的病因复杂多样, 其中遗传因素目前认为是最主要的原因, 而环境因素近几年越来越受到重视。能被病因诊断的POF患者极少, 大量研究专注于寻找POF形成的相关基因。改善低雌激素引起的症状, 尽可能恢复患者生育功能是POF的主要治疗原则。

关键词: 卵巢早衰(POF); 病理生理; 病因; 诊断; 治疗

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Premature Ovarian Failure: Current Outlook

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【ABSTRACT】 Premature ovarian failure (POF) is a grand challenge in reproductive endocrinology. The disruption in the course of follicle formation and development would lead to POF. The etiology of POF is multiple and complex. Genetic factor is thought to be the main reason for POF by now and the environmental factor is more and more concerned recently. Only a few patients of POF could be etiological diagnosed. A large quantity of researches have been designed to explore the relative genes of POF. Improving the symptoms with low estrogen and recovering the fertility as far as possible are the main treatment for POF.

Key words: premature ovarian failure (POF); pathophysiology; etiology; diagnosis; therapy

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人类辅助生殖技术中胚胎质量评估方法的研究进展

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【摘要】 胚胎质量评估方法的优劣直接关系到辅助生殖临床妊娠结局的好坏。目前, 对胚胎质量评估的方法中, 应用最广泛的是对配子、胚胎各时期的形态特征进行评分的形态学评价法; 近来, 在形态学评分系统的基础上, 结合实时成像分析系统对胚胎发育过程进行连续观察并对胚胎进行选择, 其应用价值已得到确认。而通过测定卵泡液及培养基中代谢物的代谢组学法虽然能更有效地分析胚胎活性、预测临床结局, 但因受检测技术手段的限制, 该方法尚未广泛应用于临床。且形态学和代谢组学分析不能确定染色体的异常, 因此, 染色体筛查已成为选择活力胚胎的方法之一, 但是该法会对胚胎造成损伤及结果偏差较大, 其应用还需要进一步评估。

关键词: 胚胎发育; 代谢组学; 基因组学; 植入前非整倍体筛查

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Research Progress of Embryo Quality Evaluation in Human Assisted Reproductive Technology

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【ABSTRACT】 Optimal or slight method on embryo quality evaluation is directly related to the clinical pregnancy outcome of assisted reproduction. Currently, in the embryo quality evaluation, the most widely used method is morphological evaluation method which is grading the morphological characteristics of gamete and embryo in each period. Recently, the embryo selection accords to continuous observation of the embryonic development process by morphological grading system combined with the time-lapse imaging analysis system, which application value has been recognized. The metabonomics method according to determination of the metabolites in follicular fluid and culture medium is more efficient than others on the activity analysis of embryo and predication of clinical outcome. Nevertheless, it is not widely used in the clinic due to the limitation of detection technology. Morphological and metabonomics analysis can not determine whether the chromosomal is normal or not, consequently, the chromosome screening has been one of methods in selecting viable embryo. Its application needs to be further evaluated because the method has large damage on embryo and the result deviation is more large.

Key words: embryonic development; metabonomics; genomics; preimplantation genetic screening for aneuploidy (PGS)

• 临床报道 •

宫、腹腔镜联合手术治疗剖宫产术后 子宫瘢痕憩室

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【摘要】目的: 探讨剖宫产术后子宫瘢痕憩室应用宫、腹腔镜联合手术治疗的临床效果。方法: 选择经彩色多普勒超声诊断子宫瘢痕憩室, 有手术指征的患者 17 例, 在全麻下进行宫、腹腔镜联合手术, 分离子宫膀胱反折腹膜, 切除憩室病灶, 重新缝合子宫肌层。结果: 17 例患者手术顺利, 平均手术时间为 $69.2 \pm 28.7(35 \sim 110)$ min, 术后临床症状消失, 6 个月后复查超声肌层连续, 肌壁厚度为 $1.35 \pm 0.28(0.8 \sim 1.8)$ cm, 与术前的肌壁厚度 $0.33 \pm 0.10(0.17 \sim 0.5)$ cm 相比, 差异有统计学意义($P < 0.05$)。结论: 宫、腹腔镜联合手术治疗剖宫产术后子宫瘢痕憩室安全, 微创, 效果确切。

关键词: 剖宫产; 憩室; 宫腔镜; 腹腔镜

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Hysteroscopy Combined with Laparoscopy in Treatment of Cesarean Section Scar Diverticulum

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【ABSTRACT】 Objective: To investigate the clinical effect of hysteroscopy combined with laparoscopy in treatment of cesarean section scar diverticulum. **Methods:** There were 17 patients diagnosed by the color Doppler ultrasound with uterine scar diverticulum, all had the operation indication. Hysteroscopy combined with laparoscopy operation was performed under general anesthesia. The bladder and uterus reflexed peritoneal lesions were separated, the diverticulum was resected, and the uterine myometrium was restricted. **Results:** After operation, the postoperative clinical symptoms had disappeared. Average operation time was 69.2 ± 28.7 (35–110) min. The average muscle layer thickness was 1.35 ± 0.28 (0.8–1.8) cm after 6 months of operation, and was significantly thicker than that of preoperative muscle layer [0.33 ± 0.10 (0.2–0.5) cm]. **Conclusion:** Hysteroscopy combined with laparoscopy in treatment of cesarean section scar diverticulum was safe, minimally invasive and effective.

Key words: cesarean; diverticulum; hysteroscopy; laparoscopy

65例剖宫产后切口瘢痕妊娠病例 诊疗回顾性研究

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【摘要】目的: 探讨介入治疗在子宫下段剖宫产后切口瘢痕处妊娠(cesarean scar pregnancy, CSP)的价值。方法: 回顾性分析65例CSP患者的诊疗过程, 按治疗方案分为直接手术组(A组, $n=23$)、介入+手术组(B组, $n=21$)、介入+化疗+手术组(C组, $n=8$)、化疗+手术组(D组, $n=7$)和直接化疗组(E组, $n=6$)。比较各组患者的治疗情况。结果: B、C组患者的胚囊大小、胚芽直径、血流指数、治疗前血 β -hCG水平均显著高于其他各组, 但手术出血量显著低于其他各组, D组患者的住院天数、住院金额均显著低于B、C组($P<0.05$)。结论: 针对术前胚囊较大、血流丰富、血 β -hCG水平较高的患者, 介入+手术治疗子宫下段剖宫产后切口瘢痕处妊娠能显著减少患者出血量, 效果良好。

关键词: 介入治疗; 切口妊娠; 化疗

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A Retrospective Study on 65 Cases of Patients with Cesarean Scar Pregnancy

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【ABSTRACT】 Objective: To discuss the efficacy of uterine arterial embolization on cesarean scar pregnancy (CSP). **Methods:** A retrospective study was performed to analyze the treatment outcomes of 65 CSP cases. All the patients were divided into 5 groups according to treatment methods which included surgery group (group A, $n=23$), embolization plus surgery group (group B, $n=21$), embolization initially plus chemotherapy plus surgery group (group C, $n=8$), chemotherapy plus surgery group (group D, $n=7$) and chemotherapy group (group E, $n=6$). **Results:** There were significant differences between embolization and non-embolization groups while comparing their diameters of buds, the distance between implanted site and uterine surface, serum β -hCG levels before treatments and the bleeding volume of curettage. There was a significant difference of resident duration time and medical fees between embolization and non-embolization groups ($P<0.05$). **Conclusion:** It is very effective to treat cesarean scar pregnancy with a transvascular embolization therapy, especially in cases who have bigger diameters of buds, higher serum β -hCG levels, and richer blood flow.

Key words: transvascular therapy; cesarean scar pregnancy (CSP); chemotherapy

IVF-ET后妊娠并发粟粒性肺结核 3例病案报道并文献复习

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【摘要】目的: 探讨IVF-ET后妊娠并发粟粒性肺结核的发生规律、疾病特点和检查治疗的方法。方法: 回顾分析3例IVF-ET后妊娠并发粟粒性肺结核病例的疾病特点和诊治方法。结果: 本文3例加文献7例共10例IVF-ET并发粟粒性肺结核患者, 均行IVF-ET受孕, 主要临床表现为发热, 可伴有发冷、寒战等症状, 可查的结核菌素实验均为阴性。10例患者中通过胸片诊断4例, 通过胸部CT诊断4例, 均为粟粒性小结节。从发热至影像学确诊的时间间隔, 最短11 d, 最长达9周。10例患者中9例患者在经系统抗结核治疗后病情好转, 预后良好, 仅本研究的1例患者出现昏迷, 目前遗留智力障碍。10例中主动终止妊娠2例, 出现流产情况7例, 胎儿存活3例。结论: IVF-ET并发粟粒性肺结核临床表现不典型, 给疾病的诊断带来困难。IVF-ET妊娠后, 对持续较长时间的不明原因发热、抗生素治疗无效的孕妇, 应尽早进行结核病相关检查。

关键词: 体外受精-胚胎移植(IVF-ET); 粟粒性肺结核; 女性生殖器结核(GTB)

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Miliary Tuberculosis in the *in vitro* Fertilization-embryo Transfer Pregnancy with 3 Cases Reports and Review of the Literature

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【ABSTRACT】 Objective: To study the occurrence regularity, characteristics and methods of examination and treatment of miliary tuberculosis combined with *in vitro* fertilization-embryo transfer (IVF-ET) pregnancy. **Methods:** A retrospective analysis of 3 cases who were pregnant after IVF-ET combined with miliary tuberculosis were performed, the characteristics of the disease and the diagnosis and treatment methods were analyzed. **Results:** Ten cases was analyzed, among which 3 cases were diagnosed in Shengjing Hospital of China Medical University and the domestic clinical data of the other 7 cases reported since 1994 were studied by literature review. They were all pregnant by IVF-ET, and fever was the main symptom. Tuberculin test was negative. Four cases were diagnosed by chest X-ray and 4 cases by chest CT through small miliary nodules appearance. The time interval from fever to imaging diagnosis form was 11 d in the shortest, for up to 9 weeks. Nine patients of 10 got better by the systemic anti-TB treatment, and the prognosis was good, but only 1 patient remained comatose state. Two patients with active termination of pregnancy in 10 cases and 7 cases with miscarriage, and 3 fetal cases survived. **Conclusion:** Clinical manifestations of IVF-ET concurrent miliary tuberculosis are not typical. For pregnant women, the diagnosis of the diseases was difficult. Women who had pregnancy after IVF-ET and suffered a long-time unexplained fever, and had no responded to antibiotic therapy, should be carried out as soon as possible to TB-related inspection.

Key words: *in vitro* fertilization-embryo transfer (IVF-ET); miliary tuberculosis; female genital tuberculosis (GTB)

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