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实验研究。

## γ-氨基丁酸(GABA)通过调节细胞增殖 参与小鼠胎盘的形成

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【摘要】目的: 探讨γ- 氨基丁酸(GABA)信号对小鼠胎盘形成的影响。方法: 免疫组织化学检测妊娠小鼠第9日至第14日(D9~14)胎盘中GABA的表达,对D7~13 孕鼠腹腔注射 0.04 g/kg、0.20 g/kg、1.00 g/kg GABA, D 14时称量各组胎盘和胚胎, HE染色观察胎盘形态学变化,免疫组织化学检测增殖细胞核抗原(PCNA)表达情况。结果: GABA主要表达于D9的外胎盘锥(ecto-placental cone, Epc)、D10 的绒毛膜板(chorionic plates, Cp)和 D11~14 的海绵滋养细胞层(spongiotrophoblast, Sp)。与对α (生理盐水)比较,不同浓度的 GABA 处理组的胚胎质量均显著下降(P<0.001),胎盘蜕膜区明显增厚,而海绵滋养层变得较密集并失去海绵样结构,随着 GABA 浓度增加,迷路滋养层变薄,胎儿血窦及母体血管减少。同时,0.20 g/kg和1.00 g/kg GABA处理组的蜕膜区、海绵滋养层和迷路滋养层中处于增殖期的细胞数量明显增多,差异有极显著统计学意义(P<0.001)。结论: GABA可能通过调节蜕膜细胞和滋养层细胞的增殖,从而参与了小鼠胎盘的形成过程。

关键词: γ-氨基丁酸(GABA); 胎盘形成; 增殖

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## γ-amino butyric acid (GABA) is Involved in the Mouse Placentation by Regulating the Cell Proliferation

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**(ABSTRACT) Objective**: To study the potential role of γ-amino butyric acid (GABA) in mouse placentation. **Methods**: Immunohistochemistry was applied to detect the expression of GABA in mouse placentas on D 9–14 of pregnancy. Pregnant mice were received daily intraperitoneal injections of GABA at concentrations of 0.04 g/kg, 0.20 g/kg and 1.00 g/kg, respectively from D 7 to D 13. The weight of embryos and placentas was measured and the structure of placenta was examined by HE staining on D 14. Besides, the proliferation of placenta was evaluated by expression level of proliferating cell nuclear antigen (PCNA) using immunohistochemistry. **Results**: GABA was mainly located in ecto-placetal zone (Epc) of placenta on D 9, Cp on D 10 and spongiotrophoblast (Sp) from D 9 to D 14. The weight of embryos significantly decreased in different concentration groups of GABA compared with control groups (*P*<0.001). Surprisingly, the proliferation of decidual cells and trophoblast cells in Sp zone and labyrinth zone was abnormally obvious in concentrations of GABA with 0.20 g/kg and 1.00 g/kg group compared with control groups (*P*<0.001). At the same time, the fetal and maternal blood sinusoids were reduced in labyrinth, and the structure of Sp was abnormal by HE staining. **Conclusion**: GABA may play an important role in mouse placentation via regulating the proliferation of decidua basalis and spongiotrophoblast cells.

**Key words**: γ-amino butyric acid (GABA); placentation; proliferation

## 激光皱缩法在囊胚玻璃化冷冻中的应用价值

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【摘要】目的: 探讨激光打孔使囊胚腔皱缩在体外受精周期囊胚玻璃化冷冻中的应用价值。方法: 将常规取卵后第 3 日移植、冷冻后剩余的形态学评分较差的胚胎发育而来的囊胚,采用或不采用激光打孔使囊胚腔皱缩后冷冻。分析 606 例解冻囊胚周期, 比较采用和未采用激光皱缩 2 种方法冻存囊胚的效率,分析激光皱缩在囊胚玻璃化冷冻中的价值。结果: 激光皱缩组解冻 247 例, 4 例 (1.62%)取消移植,移植 243 例; 未皱缩组 359 例, 24 例(6.69%)取消移植,移植 335 例。移植患者的年龄、不孕原因、排卵日内膜厚度、平均移植胚胎数组间均无统计学差异(P>0.05)。激光皱缩组冻融取消率和流产率均显著低于非皱缩组(P<0.05), 生化妊娠率(45.68% vs 35.82%)、种植率(22.54% vs 16.56%)和继续妊娠率(87.50% vs 75.56%)显著高于非皱缩组(P<0.05), 临床妊娠率激光皱缩组略高于非皱缩组(32.92% vs 26.87%), 但无统计学差异(P>0.05)。结论: 囊胚冷冻前采用激光打孔皱缩可提高解冻后的胚胎存活率,并能显著降低流产率。

关键词: 体外受精(IVF); 激光皱缩; 囊胚冷冻; 玻璃化

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### Application Value of Laser Drilling for Blastocoeles Shrinkage Prior to Blastocyst Vitrification in IVF Cycles

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**[ABSTRACT]** Objective: To explore the application value of laser drilling for blastocoeles shrinkage before blastocyst vitrification in *in vitro* fertilization (IVF) cycles. **Methods**: A total of 606 frozen-thawed blastocyst transfer cycles were collected. All the blastocysts were developed from day 3 embryos with low morphological scores. The application value of laser shrinkage in the blastocyst vitrification was analyzed. **Results**: There were 247 frozen-thawed cycles in laser shrinkage group, of which 4 cycles (1.62%) were cancelled for degeneration of the thawed blastocysts, and 243 cycles got embryos transfer. There were 359 cases in non-shrinkage group, 24 cases were cancelled (6.69%), 335 cases got embryos transfer. There was no difference of the patients age, the cause of infertility, endometrium thickness on ovulation day, average number of the embryos transferred between the two groups. Cancellation rate and abortion rate of laser shrinkage were significantly lower than those *in non-shrinkage group* (*P*<0.05), biochemical pregnancy rate (45.68% *vs* 35.82%), implantation rate (22.54% *vs* 16.56%) and ongoing pregnancy rate (87.50% *vs* 75.56%) were higher than those in non-shrinkage group (*P*<0.05), and clinical pregnancy rate was higher in shrinkage group than in non-shrinkage group (32.92% *vs* 26.87%), with no significant difference (*P*>0.05). **Conclusion**: Adopting laser drilling for blastocoeles shrinkage before blastocyst vitrification can improve survival rate of frozen-thawed blastocysts, reduce abortion rate significantly.

Key words: in vitro fertilization (IVF); laser shrinkage; blastocyst cryopreservation; vitrification

## 血管内皮生长因子(VEGF)及其可溶性受体在 早期复发性流产患者中的表达及临床意义

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【摘要】目的: 探讨血管内皮生长因子(VEGF)及其可溶性受体(sflt-1)与复发性流产(RSA)的相关性。方法: 应用酶联免疫吸附试验(ELISA)技术和免疫组织化学方法分别检测 30 例 RSA 患者血清和绒毛中VEGF及sflt-1的表达情况,并以同期因非意愿妊娠要求行人工流产术的正常早孕妇女(n=30)为对照,比较 VEGF及 sflt-1表达的临床意义。结果: RSA 组血清 VEGF(2 637.50 ± 2 145.09 ng/L)、sflt-1蛋白(13 796.67 ± 11 917.08 ng/L)表达水平均高于对照组(分别为 982.67 ± 675.47 ng/L和 3 540.67 ± 2 989.80 ng/L)(P<0.05); RSA 组绒毛组织 VEGF和 sflt-1的表达阳性率(分别为 76.7%和 96.7%)均高于对照组(分别为 50.0%和 66.7%)(P<0.05)。结论: RSA 患者血清和绒毛中 VEGF、sflt-1表达程度升高,可能是导致孕早期胚胎停育的原因之一。

关键词: 复发性流产(RSA); 血管内皮生长因子(VEGF); VEGF可溶性受体(sflt-1); 酶联免疫吸附试验(ELISA); 免疫组织化学

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### **Expression and Clinical Significance of VEGF and VEGF Soluble Receptor-1** in Patients of Early Recurrent Abortion

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**ABSTRACT** Objective: To explore the relationship between early recurrent spontaneous abortion (RSA) and vascular endothelial growth factor (VEGF), VEGF soluble receptor (sflt-1). Methods: Serum levels of VEGF and sflt-1 in 30 healthy early pregnancy controls of voluntary induced abortion and 30 patients of RSA were detected by ELISA. Histological localization and quantitative analysis of VEGF and sflt-1 in their chorionic villi were detected by immunohistochemistry after induced abortion. Results: The expression levels of VEGF and sflt-1 in both serum and chorionic villus tissue in RSA patients were significantly higher than those of the healthy controls (P<0.05). Serum levels of BEGF (2 637.50 ± 2 145.09 ng/L) and sflt-1 (13 796.67 ± 11 917.08 ng/L) in RSA group were significantly higher than those in the control (982.67  $\pm$  675.47 ng/L, 3 540.67  $\pm$  2 989.80 ng/L)(P<0.05). The positive rates of VEGF and sft-1 in chorionic villi tissues of RSA patients (76.7%, 96.7%) were also significantly higher than those of the control (50.0%, 66.7%)(P<0.05). Conclusion: The high expression level of VEGF and sflt-1 protein in both serum and chorionic villus tissue in RSA patients may be involved in the pathogenesis of embryo growth arrest.

**Key words**: recurrent spontaneous abortion (RSA); vascular endothelial growth factor (VEGF); VEGF soluble receptor (sflt-1); enzyme linked immunosorbent assay (ELISA); immunohistochemistry

• 临床研究•

## 子宫内膜单胺氧化酶A(MAO-A)在反复 IVF-ET失败患者种植窗口期的表达及其意义

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【摘要】目的:探讨子宫内膜单胺氧化酶 A(MAO-A)在评估子宫内膜容受性中的作用。方法:应用实时荧光定量 PCR 和免疫组织化学技术,检测 3次 IVF-ET 失败患者(A 组, n=39)、2次 IVF-ET 失败,第 3次获得临床妊娠患者(B 组, n=8)、首次 IVF-ET 获得临床妊娠患者(C 组, n=21)在子宫内膜种植窗口期子宫内膜MAO-A mRNA的表达和MAO-A 蛋白的表达及定位,同时扫描电子显微镜观察子宫内膜的胞饮突数量及发育情况,探讨子宫内膜MAO-A 在评估子宫内膜容受性中的作用。结果: 反复 IVF-ET 失败患者在子宫内膜种植窗口期子宫内膜 MAO-A 的表达低于首次 IVF-ET 获得临床妊娠的患者(P<0.05)。结论: 子宫内膜 MAO-A 可以作为子宫内膜容受性的预测指标。

关键词: 反复体外受精-胚胎移植(IVF-ET)失败; 子宫内膜容受性; 单胺氧化酶 A(MAO-A); 胞饮突

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## **Expression and Significance of Endometrial MAO-A during the Endometrial Implantation Window in Repeated IVF-ET Failure Patients**

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**[ABSTRACT]** Objective: To investigate the expression of endometrial monoamine oxidase A (MAO-A) in repeated IVF-ET failure patients, and to explore the role of MAO-A in the assessment of endometrial receptivity during the endometrial implantation window. Methods: Real-time fluorescence quantitative PCR and immunohistochemical techniques were used to detect the endometrial MAO-A mRNA expression and MAO-A protein expression and localization in the patients (group A: who failed in IVF-ET three times; group B: who failed in IVF-ET two times, but succeed in the third IVF-ET; group C: who succeed in the first IVF-ET) during the endometrial receptivity window. Moreover the quantity and development of the endometrial pinopodes were obsered by scanning electron microscopy in order to explore the role of MAO-A in the assessment of endometrial receptivity. Results: MAO-A expression of the the repeated IVF-ET failure patients was significantly lower than that of the patients who successfully got pregnant in the first IVF-ET during the endometrial receptivity window, and the difference was statistically significant (P < 0.05). Conclusion: Endometrial MAO-A is a predictor of endometrial receptivity.

**Key words**: repeated *in vitro* fertilization-embryo transfer (IVF-ET) failure; monoamine oxidase A (MAO-A); endometrial receptivity; endometrial pinopodes

## 体外受精-胚胎移植周期透明带透亮致密患者 的受精与临床结局

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【摘要】目的: 探讨卵子透明带透亮致密患者行常规体外受精(IVF)或卵胞质内单精子显微注射(ICSI)后受精、胚胎发育情况及临床结局。方法: 回顾性分析体外受精过程中卵子出现透明带透亮致密的 43 个周期, 其中 IVF周期 27 例, ICSI 周期 16 例, 比较受精率与正常受精比例、胚胎质量、临床妊娠结局。结果: 27 例 IVF周期均未受精, 行早期补救 ICSI, 其中 23 例完全不受精。补救后 IVF总体受精率达 64.83%, 正常受精率 59.32%; 16 例 ICSI 周期均受精, 受精率和正常受精率分别为 85.11%和79.01%, 均显著高于 IVF组(P<0.05)。 IVF组和 ICSI 组卵裂率分别为 97.96%、95.65%, 优质胚胎率分别为 52.67%、43.75%, 组间差异无统计学意义(P>0.05)。 IVF组妊娠率为 37.04%, 种植率为 33.33%; ICSI 组妊娠率为 31.25%, 种植率为 25.00%, 组间临床结局相近, 无统计学差异(P>0.05)。 结论: 透明带透亮致密患者的自然受精能力下降, 需要采用 ICSI 方式授精。常规 IVF 受精失败后采用早期补救 ICSI 或直接行 ICSI 能明显改善透明带透亮致密患者的受精结局, 但不能改善妊娠结局。

关键词:透明带异常;受精方式;胚胎发育;临床结局

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## Fertilization Results and Clinical Outcome of Oocyte with Abnormal Zona Pellucida in IVF-ET

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**[ABSTRACT] Objective**: To explore the fertilization result, embryo development and the clinical outcome of oocytes with abnormal zona pellucida after conventional *in vitro* fertilization (IVF) or intracytoplasmic sperm injection (ICSI). **Methods**: A retrospective analysis was performed on a total of 43 cycles with abnormal zona pellucida. There were 27 IVF cycles and 16 ICSI cycles. The fertilization rate, the normal fertilization rate, the quality of the embryo and the clinical pregnancy rate were compared between IVF and ICSI. **Results**: Recuse ICSI was applied to 27 IVF cycles which failed to extrude the second polar body after conventional IVF, and of which 23 IVF cycles completely failed; but all the ICSI cycles succeeded to fertilize. The fertilization rate and the normal fertilization rate of IVF (64.83%, 59.32%) were significantly lower than those of ICSI (85.19%, 79.01%), and the cleavage rate (97.96%) was higher than that of ICSI group (95.65%), but no significant difference was observed (*P*>0.05). The formation rate of good-quality embryos resulting from the oocytes with abnormal zona pellucida in IVF group was 52.67%, while that of ICSI was 43.75%, no significant difference was observed (*P*>0.05). The pregnancy rate and the implantation rate of IVF group (37.04%, 33.33%) were higher than those of ICSI group (31.25%, 25.00%, *P*>0.05), with no significant difference. **Conclusion**: ICSI and rescue ICSI should be carried out for those oocytes with abnormal zona pellucida for high risk of IVF failure. Recuse ICSI improves the fertilization results, but it can not improve the clinical outcome of oocytes with abnormal zona pellucida.

Key words: abnormal zona pellucida; fertilization methods; development of embryo; clinical outcome

# IVF-ET治疗周期中卵泡提前黄素化的相关因素分析

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【摘要】 目的: 初步探讨控制性超促排卵(COH)过程中如何避免卵泡提前黄素化(premature luteinization, PL),提高 IVF-ET 妊娠率。方法: 回顾性分析行 GnRH-a 黄体中期长方案的 IVF-ET 治疗患者的临床资料,共2355个周期,根据 hCG 注射日孕酮(P)/雌二醇(E2)水平的比值是否>1分为 PL组: 即卵泡提前黄素化组, P/E2 $\geq$ 1,共63个周期;非 PL组: 即卵泡未提前黄素化组, P/E2<1,共2292个周期。比较患者的一般资料及 COH 的参数资料,分析可能与 PL相关的因素。结果: PL在 GnRH-a 长方案 IVF-ET 患者中的发生率为 2.68%。 女方年龄、 男方年龄、 女方体质量指数(BMI)、基础 E2(bE2)、 bLH、 bFSH、 不孕年限、治疗周期数、 Gn 启用剂量、 hMG 使用总量、 hMG 使用总 天数、 hCG 注射日 LH 值组间差异无统计学意义(P>0.05)。 PL 组的 Gn 使用总量及 Gn 使用天数比非 PL 组的高,差异有统计学意义(P<0.05)。 PL 组的 hCG 注射日直径>15 mm 卵泡数及 M<sub>II</sub> 卵数比非 PL 组的少,差异有统计学意义(P<0.05)。 结论: PL 在行 GnRH-a 长方案的 IVF-ET 治疗患者中的发生率为 2.68%。 Gn 的使用天数、 Gn 总量过多,卵巢低反应可能是发生 PL 的相关因素,为避免发生 PL 可适当减少 Gn 的使用天数及 Gn 使用总量。

关键词: IVF-ET; 卵泡提前黄素化(PL); 控制性超促排卵(COH)

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## Potential Causes of Premature Luteinization during the Treatment of *in vitro* Fertilization-embryo Transfer (IVF-ET)

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**[ABSTRACT]** Objective: To investigate how to avoid premature luteinization (PL) during controlled ovarian hyperstimulation (COH) and improve pregnancy rate. Methods: A total of 2 355 cycles who had undergone IVF-ET for infertility treatment were enrolled into the respective study. PL group consisted of the patients with PL of which P/E<sub>2</sub> ratio on human chorionic gonadotropin (hCG) administration day was  $\geq 1$  (n=63) and non-PL group consisted of the patients whose P/E<sub>2</sub> ratio was <1 (n=2 292). The differences between the two groups in clinical parameters were compared. Results: The incidence rate of PL was 2. 68%. The differences had no statistical significance between the two groups in the female age, male age, woman's body mass index (BMI), the basic levels of E<sub>2</sub>, LH, FSH, the duration of infertility, treatment cycles, initial dasages of gonadotropin (Gn), total dosages of hMG used, duration of hMG stimulation, serum LH level on the day of hCG injection (P>0.05). But the total dosages of Gn used and duration of Gn used in PL group were significantly higher than those in non-PL group (P<0.05). The number of follicles with the diameter> 15 mm on the hCG injection day and the number of M<sub>II</sub> egg in PL group were less than those in non-PL group (P<0.05). Conclusion: The total dosages of Gn used, the duration of Gn used, poor ovarian response may be relate to the PL. To reduce the incidence of PL, we had better decrease the total dosages of Gn used and the dosage of Gn started.

Key words: IVF-ET; premature luteinization (PL); controlled ovarian hyperstimulation (COH)

## 育龄女性血清硫酸脱氢表雄酮(DHEA-S) 检测分析及其临床意义

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【摘要】目的:探讨月经正常的不同年龄段育龄女性血清硫酸脱氢表雄酮(DHEA-S)水平变化及其临床应用意义。方法: 1 156 名月经正常且年龄在 21~45 周岁的育龄女性为研究对象,按年龄分成 5组,检测血清 DHEA-S、bFSH、bLH及实卵泡计数(AFC)水平。结果:年龄段在 21~25 岁、26~30 岁、31~35 岁、36~40 岁、41~45 岁妇女的血清 DHEA-S 90% 正常参考值范围分别为 3.42~10.42 µmol/ml、3.27~10.20 µmol/ml、2.59~10.14 µmol/ml、2.26~8.08 µmol/ml、2.14~7.50 µmol/ml。不同年龄组间血清 DHEA-S水平比较差异有统计学意义(P<0.01),血清 DHEA-S与年龄呈负相关,差异有统计学意义(r=-0.28,95% CI=5.78~6.03, P<0.01); 血清 DHEA-S与 bFSH和 bFSH/LH均呈负相关,DHEA-S与 AFC 呈正相关,差异均有统计学意义,r 分别为 -0.13、-0.08、0.592,95% CI分别为 7.53~7.89、1.67~1.82、13.90~14.93, P<0.01。结论:随年龄增大,血清 DHEA-S 水平下降,可作为评估卵巢储备功能的一项参考指标,为临床诊治提供参考。

关键词: 硫酸脱氢表雄酮(DHEA-S); 90% 正常参考值; 基础卵泡刺激素(bFSH); 基础卵泡刺激素/ 黄体生成素(bFSH/bLH); 窦卵泡计数(AFC)

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## Detection of Serum Dehydroepiandrosterone Sulfate (DHEA-S) Levels in Reproductive Women and Its Clinical Significance

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**[ABSTRACT] Objective**: To explore serum dehydroepiandrosterone sulfate (DHEA-S) concentrations in reproductive women of different age with regular menstruation and its clinical significance. **Methods**: Totally 1 156 reproductive women aged 21–45 years old were enrolled. Subjects were divided into five groups by age, antral follicular count (AFC) and serum levels of DHEA-S, bFSH, bLH were detected. **Results**: The 90% normal reference value range of DHEA-S was  $3.42-10.42~\mu$ mol/ml in group of age from 21 to 25 years old,  $3.27-10.20~\mu$ mol/ml in group of age from 26 to 30 years old,  $2.59-10.14~\mu$ mol/ml in group of age from 31 to 35 years old,  $2.26-8.08~\mu$ mol/ml in group of age from 36 to 40 years old,  $2.14-7.50~\mu$ mol/ml in group of age from 41 to 45 years old. The serum DHEA-S levels between different age groups had significant differences (P<0.01). The serum DHEA-S level was negatively correlated with age (r=-0.28, 95%CI=5.78-6.03, P<0.01). In addition, there was a negative correlation between DHEA-S and bFSH, bFSH/LH (r=-0.13, 95%CI=7.53-7.89; r=-0.08, 95%CI=1.67-1.82, P<0.01), and a positive correlation between DHEA-S and AFC (r=0.592, 95%CI=13.90-14.93, P<0.01), the differences were statistically significant. **Conclusion**: As the age increased, serum DHEA-S levels decreased. Serum DHEA-S levels can be used as an indicator to evaluate the ovarian reserve function, and provide reference for clinical medication.

**Key words**: dehydroepiandrosterone sulfate (DHEA-S); normal reference value range; bFSH; bFSH/LH; antral follicular count (AFC)

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• 综述 •

## 体外诱导人胚胎干细胞向滋养层细胞 分化的研究进展

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【摘要】目前在体外研究中,主要通过分离胚体和骨形态发生蛋白 4(bone morphogenetic protein 4, BMP4)诱导这 2种途径从人胚胎干细胞(hESC)分化获取滋养层细胞(TB)。胚体途径可基于细胞的黏附性和培养基中β-hCG的含量从胚体中分离获得TB,进而在三维培养体系中可检测细胞的侵袭性及细胞与基质的相互作用。BMP4途径通过去除外源性成纤维细胞生长因子及提高氧含量均可促进 BMP4 诱导 TB 的分化。虽然 hESC 分化 TB 模型目前还存在一些争议,但是相关研究可为探讨人类胚胎的植入及胎盘的形成提供重要的理论依据。

关键词: 人胚胎干细胞(hESC); 滋养层细胞(TB); 胚体; 骨形态发生蛋白4(BMP4); 分化

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## Research Progress in Trophoblast Differentiation from Human Embryonic Stem Cell Induced *in vitro*

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**【ABSTRACT】** Currently, trophoblasts (TBs) mainly have been differentiated from human embryonic stem cells (hESCs) by separating embryoid bodies (EBs) and bone morphogenetic protein 4 (BMP4) treatment *in vitro*. For EB-derived trophoblasts, approaches to purify them from EBs are based on selection for adhesive ability and for  $\beta$ -hCG content in the medium. The cell invasion and interaction between TB and extracellular matrix can be tested in three-dimensional culture system. For BMP4-driven trophoblasts, absence of fibroblast growth factor 2(FGF2) and a high concentration of  $O_2$  gas atmosphere can contribute to their differentiation. However, the models of hESC-derived TB remain controversial. Anyway, studies on the differentiation of TB from hESC may provide an important theoretical basis for researching human embryo implantation and placentation.

**Key words**: human embryonic stem cell (hESC); trophoblast (TB); embryoid body; bone morphogenetic protein 4 (BMP4); differentiation

## 子宫内膜局部肾素-血管紧张素系统

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【摘要】肾素-血管紧张素系统(renin-angiotensin system, RAS)是人体重要的体液调节系统,当这一系统出现紊乱易引发多种疾病。以往研究多偏重于全身 RAS系统,近年来,局部 RAS成为研究热点。子宫内膜相关研究表明,局部 RAS参与子宫内膜周期性变化及生殖功能调节、维持妊娠期人体子宫稳态等一系列生理过程;并参与子宫内膜异位症、功能性子宫内膜出血、子宫内膜癌等病理生理过程。

关键词: 肾素 - 血管紧张素系统(RAS); 血管紧张素; 血管紧张素受体; 子宫内膜

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### Local Renin-angiotensin System in Endometrium

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**【ABSTRACT】** Renin-angiotensin system (RAS) is an important humoral regulation system in human body, the disorder of this system could induce many diseases. Many previous studies focus on this circulating RAS system, local RAS becomes a research hotspot these years. Related studies have shown that local RAS participates in a series of physiological processes such as endometrial periodic changes, reproductive function regulation, and pregnant uterine body homeostasis. And local RAS also participates in the pathological process such as endometriosis (EMs), functional endometrial bleeding and endometrial cancer.

Key words: renin-angiotensin system (RAS); angiotensin; angiotensin receptor; endometrium

## 子痫前期相关microRNA的研究进展

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【摘要】子痫前期(PE)是妊娠期特发性疾病,其病因和发病机制至今仍未完全阐明。近年来有研究表明PE患者的胎盘和血循环中存在一些微小RNAs(microRNA, miRNA)与正常妊娠者存在显著性差异表达,这些miRNA的靶标可能与子痫前期的发病机制相关,如miR-210、miR-155、miR-18b与胎盘缺血、缺氧相关; miR-152、miR-19a、miR-182、miR-181a与免疫因素有关。研究PE相关miRNA及其对靶标的调控可能有助于阐明PE的发病机制。

关键词: 子痫前期(PE); 微小RNA(miRNA); 胎盘

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#### Reproduction & Contraception

#### Study Progress of MicroRNA in Preeclampsia

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**【ABSTRACT】** Preeclampsia (PE) is a pregnancy idiopathic disease. Its etiology and pathogenesis remaines unknown. In recent years, studies have shown that compared with normal pregnancies, some miRNAs expressions are different in placentas and peripheral circulation of patients with preeclampsia. The targets of these miRNAs are associated with the pathogenesis of preeclampsia. It was reported that miR-210, miR-155 and miR-18b were associated with ischemia and anoxia of the placenta; miR-152, miR-19a, miR-182 and miR-181a were associated with the immune factors of PE. To study the function of miRNAs may contribute to elucidate the pathogenesis of PE.

Key words: preeclampsia (PE); microRNAs (miRNAs); placenta

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• 临床报道•

## 甲状腺自身抗体阳性对体外受精-胚胎移植结局的影响

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【摘要】目的: 探讨抗甲状腺自身抗体(antithyroid autoantibodies, ATA)阳性对体外受精-胚胎移植 (in vitro fertilization and embryo transfer, IVF-ET)结局的影响。方法: 回顾性分析行IVF/ICSI治疗不 孕的患者资料。选取甲状腺抗体阳性但甲状腺功能正常者65例(共71个周期)作为研究组(ATA+组), 492 例甲状腺抗体阴性患者(共512个周期)作为对照组(ATA-组)。结果: ATA+组与ATA-患者的一般情况、促排卵天数、促性腺激素使用总量(Gn总量)、hCG 注射日  $E_2$  水平、获卵数、ICSI 受精率、可移植胚胎数和妊娠率,组间比较均无统计学差异(P>0.05)。ATA+组 IVF 受精率(59.73%)、优质胚胎率(26.94%)明显低于 ATA-组(70.86% 和 36.31%); ATA+组的流产率(37.50%)明显高于 ATA-组(17.79%),差异有统计学意义(P<0.05)。结论: ATA+对 IVF-ET 妊娠结局有不利的影响,因此,对于ATA+患者在接受 IVF-ET治疗前调节甲状腺自身免疫功能可对妊娠结局有利。

关键词: 甲状腺自身抗体(ATA); 体外受精 - 胚胎移植(IVF-ET); 妊娠结局; 流产

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## Impact of Antithyroid Antibody Positive on the Outcome of In Vitro Fertilization and Embryo Transfer

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[ABSTRACT] Objective: To investigate the impact of antithyroid autoantibodies (ATA) on pregnancy outcome in the *in vitro* fertilization and embryo transfer (IVF-ET) patients. Methods: A total of 65 infertile women (71 cycles) who were antithyroid antibody positive (ATA<sup>+</sup> group) and 492 infertile women (512 cycles) who were antithyroid antibody negative (ATA<sup>-</sup> group) undergoing IVF/ICSI were retrospectively analyzed. Results: There was no significant difference in the days of ovarian stimulation, total gonadotropin dosage, serum E<sub>2</sub> level on hCG injection day, the number of oocytes retrieved, the fertility rate of ICSI, the number of available embryos and the pregnancy rate between the two groups. The IVF fertilization rate, the high-quality embryo rate were significantly lower in ATA<sup>+</sup> group than in ATA<sup>-</sup> group (59.73% *vs* 70.86%, 26.94% *vs* 36.31%). Abortion rate was significantly higher in ATA<sup>+</sup> group than in the control (37.50% *vs* 17.79%). Conclusion: The ATA positive is detrimental for the pregnancy outcome following IVF-ET. Therefore, regulating thyroid autoimmune function before and during IVF treatment may have some benefits for pregnancy outcome.

**Key words**: antithyroid autoantibodies (ATA); *in vitro* fertilization and embryo transfer (IVF-ET); pregnancy outcome; abortion

## 子宫内膜异位症与血清CA125水平相关分析

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【摘要】目的:探讨血清 CA125与子宫内膜异位症(EMs)的相关性。方法:对256例EMs患者进行回顾性分析。观察CA125与EMs分型、rAFS分期、痛经程度、子宫直肠窝封闭情况的关系。结果:①腹膜型EMs血清CA125水平显著低于卵巢型和混合型,卵巢型、混合型间差异无统计学意义;②不同临床分期间血清CA125差异均有统计学意义,期别越高血清CA125水平越高;③无痛经组血清CA125(19.5 KU/L)水平低于有痛经组(轻度:28.3 kU/L、中度:35.2 kU/L、重度:35.0 kU/L),差异有统计学意义,不同程度痛经组间血清CA125水平相当,差异无统计学意义;④子宫直肠窝无封闭组血清CA125水平显著低于部分或全部封闭组,差异有统计学意义,部分和全部封闭组血清CA125水平相当,差异无统计学意义;⑤各组间CA125的阳性率均有显著差异;⑥多因素非条件Logistic分析结果提示rAFS分期是血清CA125阳性的危险因素,分期越高血清CA125阳性的发生风险越高。结论:血清CA125对EMs病情严重程度的综合评估有重要意义,可用于协助判断EMs分型,临床上尤可用于EMs术前评价,为个体化术前处理提供参考。

关键词: 子宫内膜异位症(EMs); 分型; 临床分期; 痛经; CA125

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#### Evaluation of the Relationship between Serum CA125 Levels and Endometriosis

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**(ABSTRACT)** Objective: To explore the relationship between serum CA125 levels and endometriosis (EMs). Methods: A total of 256 patients with EMs were studied retrospectively, the relationship between CA125 and categories, rAFS stages, the intensity of dysmenorrhea, extension of adhesion in recto-vaginal pouch was explored. Results: 1) Serum CA125 levels were significantly elevated in patients with ovarian and mixed EMs lesions compared with those who had peritoneal foci. However, no statistical difference was found between ovarian and mixed EMs groups. 2) Serum CA125 levels were related to the clinical staging of EMs. CA125 levels in patients with advanced stage were higher than those in early stage. 3) There were significantly higher CA125 levels in patients with dysmenorrhea, while no statistical differences were found among mild, moderate and severe dysmenorrea groups. 4) Serum CA125 levels were significantly elevated in patients with complete and partly obliteration of cul-de sac compared with those without adhesion in culde sac. However, no statistical difference was found between complete or partly obliteration of cul-de sac groups. 5) There were significant differences in positive rates among groups. 6) Multivariate non-conditional Logistic regression analyses revealed that rAFS stage was an independent risk factor for higher serum CA125 levels. Conclusion: The CA125 is associated with the severity of EMs. Serum CA125 levels could be used to discriminate EMs categories. And serum CA125 levels have an important reference value for us to make individualized preoperative therapeutic regimen in treatment of EMs.

**Key words**: endometriosis (EMs); category; clinical stage; dysmenorrhea; CA125

## 米非司酮配伍米索前列醇与苯甲酸雌二醇在稽 留流产清宫术前应用的临床效果比较

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【摘要】目的: 探讨米非司酮配伍米索前列醇在稽留流产清宫术前的临床应用效果。方法: 回顾性分析52例米非司酮配伍米索前列醇加清宫治疗稽留流产(A组)的临床效果, 并与32例苯甲酸雌二醇加清宫治疗稽留流产者(B组)进行疗效比较。结果: A组服药后6h内胚胎排出27例(51.92%),宫颈软化扩张率为100%,手术时间为5.2 ± 1.5 min,术中出血量为19.3 ± 8.5 ml,术后出血时间为4.2 ± 1.3 d,均1次清宫成功,疼痛程度轻,均未发生人工流产综合征(0%); B组服药后6h内均未见胚胎排出(0%),宫颈软化扩张者占6.25%,清宫前需扩宫,手术时间为11.2 ± 3.5 mim,术中出血量为60.0 ± 10.6 ml,术后出血时间为10.1 ± 2.3 d, 26 例(81.25%)1次清宫成功,疼痛程度明显及人工流产综合征发生率高(13.46%);各项观察指标与A组相比,均有显著统计学差异(P<0.01)。结论:米非司酮配伍米索前列醇在稽留流产清宫术前应用是一种简便、安全、有效的方法,值得推广。

关键词: 米非司酮; 米索前列醇; 稽留流产

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## Comparison of Clinical Treatment Effect between Mifepristone Combining with Misoprostol and Estradiol Benzoate in Missed Abortion

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**[ABSTRACT] Objective**: To investigate the effect of mifepristone combining misoprostol in missed abortion. **Methods**: Totally 52 cases treated with mifepristone combining misoprostol (group A) and 32 cases treated with estradiol benzoate (group B) were retrospectively analyzed. **Results**: For group A, embryo aborted number in 6 h was 27 (51.92%), cervical softening was 100%, time in surgery was  $5.2 \pm 1.5$  min, amount of bleeding was  $19.3 \pm 8.5$  ml, postoperative hemorrhage time was  $4.2 \pm 1.3$  d, the curettage rate was 100%. For group B, embryo aborted number was 0 (0%), cervical softening was 6.25%; expanding palace was needed before curettage. Time in surgery was  $11.2 \pm 3.5$  min, amount of bleeding was  $60.0 \pm 10.6$  ml, postoperative hemorrhage time was  $10.1 \pm 2.3$  d, the number of solography of cavity was 26 (81.25%). The postoperative pain of group A was better and the incidence of abortion syndrome was lower, there was an obvious significance in the comprehensive function between the two groups (P < 0.01). **Conclusion**: It is safe and effective to apply mifepristone combining with misoprostol in missed abortion which should be widely applied.

Key words: mifepristone; misoprostol; missed abortion