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• 实验研究 •

## Rab13-蛋白激酶A途径调节体外培养支持细胞屏障通透性的研究

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**【摘要】**目的: 研究 Rab13 蛋白在支持细胞(SC)屏障功能调节中的作用。方法: 体外分离培养大鼠睾丸 SC, Western blotting 检测 Rab13 的表达, 免疫共沉淀检测 Rab13 与蛋白激酶 A(PKA)催化亚基间的相互作用; 睾酮处理建立 SC 体外屏障增强模型, Western blotting 和放射自显影法分别检测 Rab13 的表达及 PKA 活性变化, 并通过跨上皮电阻(TER)检测 PKA 活性对 SC 屏障功能的影响; 小干扰 RNA(siRNA)干扰 Rab13 表达, 检测其对 PKA 活性及 SC 屏障功能的影响。结果: Rab13 的表达随 SC 屏障的建立逐渐降低, 且与 PKA 催化亚基间存在相互作用; 睾酮处理可使 Rab13 的表达下降而 PKA 活性升高; Rab13 siRNA 干扰可导致 PKA 活性升高, 且 SC 屏障功能增强; 抑制 PKA 活性可以拮抗睾酮或 Rab13 siRNA 对屏障功能的增强作用。结论: Rab13 可通过调节 PKA 活性参与调节 SC 屏障通透性。

**关键词:** 支持细胞(Sertoli cell, SC); 血-睾屏障; Rab13; 蛋白激酶 A(PKA)

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## Study of Regulation of Sertoli Cell Barrier Permeability by *Rab13*-PKA Pathway *In Vitro*

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**【ABSTRACT】 Objective:** To investigate the role of Rab13 in Sertoli cell (SC) permeability barrier. **Methods:** SCs were isolated from 20 d-old rat testis and cultured *in vitro*; the expression of Rab13 was detected by Western blotting; the direct interaction between Rab13 and protein kinase A (PKA) was detected by CO-IP. The expression of Rab13 and the PKA activity were also studied by Western blotting and autoradiography respectively in the testosterone-induced SC barrier enhancing model; the TER was also determined to defect the effect of PKA activity on the function of SC barrier. Then RNAi was applied to reveal the relationship between Rab13 and PKA activity, and the role of Rab13 in the regulation of SC barrier. **Results:** The expression of Rab13 decreased accompanied with the construction of the SC blood-testis barrier *in vitro*. A direct interaction was observed between Rab13 and PKA catalytic subunit. The treatment of testosterone led to a decrease in Rab13 expression but an increase in PKA activity. PKA activity also increased after Rab13 siRNA treatment, which also led to an elevation of SC barrier function. However, the effects of either testosterone or Rab13 siRNA on SC permeability could be antagonized by PKA inhibitor H89. **Conclusion:** Rab13 participates in the regulation of SC permeability barrier through PKA.

**Key words:** Sertoli cell (SC); blood-testis barrier; Rab13; protein kinase A (PKA)

# 链状酰胺类化合物B07的体外杀精效果 及其对精子质膜的影响

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**【摘要】**目的: 研究一种链状酰胺类化合物(B07)的体外杀精作用及其对精子质膜的影响。方法: 上游收集高活力人类精子分别与 0  $\mu\text{g/ml}$ (对照组), 5~640  $\mu\text{g/ml}$  B07 作用 30 min, 随后用计算机辅助精液分析仪分析记录精子的活率及运动参数; 用 160  $\mu\text{g/ml}$  B07 与精子作用, 记录 5 min、30 min、60 min 和 120 min 时精子活动率; 处理后的精子一部分经 SYBR-14/PI 双染后用荧光显微镜观察, 另一部分通过电子显微镜来观察质膜的变化情况; 并以壬苯醇醚(N9)作为阳性对照。结果: 随着 B07 浓度的升高, 精子活率和活力呈下降趋势, 最低有效浓度(MEC)为 640  $\mu\text{g/ml}$ ; 荧光显微镜下经 B07 处理的精子呈橙色, 而 N9 处理的精子呈红色; 电子显微镜显示 B07 组精子头部肿胀起泡, 尾部针孔样损伤, N9 组精子呈溶解性改变。结论: B07 具有体外杀精作用, 且该作用有时间和浓度依赖性, 且其对精子质膜的影响小于 N9。

**关键词:** 链状酰胺类化合物 B07; 人类精子; 杀精; 质膜

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## Effect of B07 on Spermicidal Activity and Membrane Change of Human Sperm *In Vitro*

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**【ABSTRACT】 Objective:** To evaluate the spermicidal activity of B07 and its effect on spermatozoa membrane. **Methods:** Human spermatozoa after “swim-up” were incubated with two-fold serial dilutions of B07. The spermicidal activity of B07 was assessed by computer-assisted sperm analysis (CASA). Sperms were stained and observed under fluorescence microscope. Scanning electron microscopy was used for topographical imaging of different membrane domains over the sperms. **Results:** Sperm motility and vitality descended with the increase of B07 concentration. The minimum effective concentration of B07 that induced immobilization of human sperm was 640 µg/ml. Fluorescence microscope examination showed that B07-treated sperm appeared orange while N9-treated red. The electron micrographs of B07-treated sperm showed slightly swollen membrane with some vesiculations and visibly perforations of sperm tail. Otherwise, N9-treated sperm were acutely damaged. **Conclusion:** The *in vitro* study proved the dose- and time-dependent spermicidal activity of B07. Furthermore, the membrane-damage effect of B07 is much less than that of N9.

**Key words:** B07; human spermatozoa; spermicidal; membrane

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• 临床研究 •

## 环孢素A通过活化粘着斑激酶信号通路 促进人滋养细胞的体外生长

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**【摘要】**目的: 探讨粘着斑激酶(focal adhesion kinase, FAK)信号通路在环孢素 A(cyclosporin A, CsA)调节人滋养细胞体外生长中的作用。方法: 收集因非意愿妊娠6~9周要求行人工流产术的正常妊娠妇女的绒毛组织, 体外分离培养获得滋养细胞, 经 CsA 和 / 或 FAK 抑制剂 Y15 处理后, 免疫荧光检测滋养细胞FAK的磷酸化水平; BrdU检测滋养细胞的增殖; Annexin V/PI检测滋养细胞的凋亡。结果: CsA 可明显提高滋养细胞FAK的活化水平, FAK 抑制剂 Y15 可阻断 CsA 诱导的 FAK 活化, 阻抑 CsA 对细胞增殖的促进作用( $P < 0.05$ )以及对滋养细胞凋亡的抑制作用( $P < 0.05$ )。结论: CsA 可通过活化FAK信号通路促进人早孕期滋养细胞的体外生长, 从而有利于正常妊娠的维持。

**关键词:** 环孢素A(CsA); 滋养细胞; 粘着斑激酶(FAK); 增殖; 凋亡

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## Cyclosporin A Promotes the Growth of Human Trophoblast Cells *In Vitro* via Focal Adhesion Kinase Signaling Pathway

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**【ABSTRACT】 Objective:** To investigate the role of focal adhesion kinase (FAK) signaling pathway on cyclosporin A (CsA)-induced growth of human trophoblast cells *in vitro*. **Methods:** Human villous tissues were collected from elective termination of first trimester pregnancies (6–9 weeks of gestation) for non-medical reasons. Primary trophoblast cells were prepared by the trypsin-DNase I digestion. After treatments of trophoblast cells with CsA and/or Y15 (a specific inhibitor of FAK), the phosphorylation of FAK was detected by immunofluorescence assay, the proliferation was examined by BrdU incorporation, and the apoptosis was evaluated by Annexin V/PI staining. **Results:** CsA significantly enhanced the activation of FAK in human primary trophoblasts, and Y15 inhibited this activity of CsA. In addition, Y15 abrogated CsA-increased proliferation and *CsA-decreased apoptosis of trophoblast cells*. **Conclusion:** CsA promotes the growth of human trophoblasts *in vitro* via FAK signaling pathway which is involved in the favorable modulation of CsA on pregnancy maintenance.

**Key words:** cyclosporin A (CsA); trophoblast; focal adhesion kinase (FAK); proliferation; apoptosis

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# 血管内皮生长因子和缺氧诱导因子-1 $\alpha$ 在妊娠高血压综合征患者胎盘组织中的表达

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**【摘要】**目的: 探讨胎盘组织中血管内皮生长因子(VEGF)和缺氧诱导因子-1 $\alpha$ (HIF-1 $\alpha$ )表达水平与妊娠高血压综合征(PIH综合征)患者严重程度的相关性。方法: 采用免疫组织化学EliVision法对35例PIH综合征患者和40例正常产妇(对照组)胎盘组织中VEGF和HIF-1 $\alpha$ 的表达水平进行检测分析。结果: VEGF和HIF-1 $\alpha$ 在胎盘滋养细胞和血管内皮细胞中均有的表达, VEGF在轻度PIH综合征患者胎盘中的表达水平与对照组相比无显著差异, VEGF在中度和重度PIH综合征患者胎盘中的表达水平则较对照组显著下降( $P < 0.05$ ), HIF-1 $\alpha$ 在PIH综合征组患者胎盘中的表达水平显著高于对照组( $P < 0.05$ ), 且重度高于中度、中度高于轻度。结论: PIH综合征患者胎盘中VEGF的表达水平降低, 而HIF-1 $\alpha$ 的表达水平升高, 并均与病情的严重程度相关, 提示其可能参与调控PIH综合征的发生和发展过程。

**关键词:** 妊娠高血压综合征(PIH综合征); 胎盘; 血管内皮生长因子(VEGF); 缺氧诱导因子-1 $\alpha$ (HIF-1 $\alpha$ )

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## Expression of VEGF and HIF-1 $\alpha$ in Placentas of Pregnancy Induced Hypertension Syndrome Patients

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**【ABSTRACT】 Objective:** To explore the correlation between the expression levels of vascular endothelial growth factor (VEGF)/hypoxia inducible factor -1 $\alpha$  (HIF-1 $\alpha$ ) and pathogenesis of pregnancy induced hypertension (PIH). **Methods:** The semi-quantitative immunohistochemical EliVision analysis was used to detect the expression of VEGF and HIF-1 $\alpha$  in placental tissues of 35 PIH patients and 40 normal pregnant women. **Results:** The expression of VEGF and HIF-1 $\alpha$  was observed in trophoblast cells and vascular endothelial cells. The VEGF expression level of mild PIH group showed no significant difference; whereas its expression levels of moderate and severe PIH groups were significantly decreased compared with control group ( $P<0.05$ ). The HIF-1 $\alpha$  expression levels of mild, moderate and severe PIH groups were significantly increased compared with control group ( $P<0.05$ ); furthermore, the HIF-1 $\alpha$  expression level of moderate group was remarkably higher than that of mild group ( $P<0.05$ ), but obviously lower than that of severe group ( $P<0.05$ ). **Conclusion:** The VEGF expression level in placentas of PIH patients was decreased, while the expression level of HIF-1 $\alpha$  was increased, indicating that VEGF and HIF-1 $\alpha$  might be involved in the pathogenesis of PIH.

**Key words:** pregnancy induced hypertension (PIH) syndrome; placenta; vascular endothelial growth factor (VEGF); hypoxia inducible factor-1 $\alpha$  (HIF-1 $\alpha$ )

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## 缩宫素受体拮抗剂阿托西班在囊胚 解冻移植中的临床观察

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**【摘要】**目的: 探讨缩宫素受体拮抗剂阿托西班在囊胚解冻移植中的作用。方法: 回顾性分析 264 例行冻融囊胚移植患者的临床资料, 移植前行单剂量阿托西班(6.75 mg/0.9 ml, iv)预处理者为研究组( $n=117$ ), 移植前未使用阿托西班预处理者为对照组( $n=147$ )。结果: 研究组的胚胎着床率(53.1%)明显高于对照组(40.1%), 差异有统计学意义( $P=0.003$ ); 研究组临床妊娠率(66.7%)亦明显高于对照组(55.4%), 差异有统计学意义( $P=0.041$ )。结论: 囊胚解冻移植前给予阿托西班预处理可明显改善患者的妊娠结局。

**关键词:** 缩宫素受体拮抗剂; 冻融; 囊胚; 移植; 妊娠率

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## Clinical Study of Oxytocin Antagonist Atosiban in Blastcyst Thawed Embryo Transfer

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**【ABSTRACT】Objective:** To investigate the use of an oxytocin antagonist atosiban in improving the pregnancy outcome of blastcyst thawed embryo transfer. **Methods:** A total of 264 infertile couples undergoing bTET were retrospectively studied. They were divided into two groups. Patients in study group received a single bolus dose (6.75 mg/0.9 ml, iv) of atosiban before bTET ( $n=117$ ), patients who did not receive atosiban were used as the control ( $n=147$ ). **Results:** A significantly higher implantation rate was noted in the control compared with study group (53.1% vs 40.1%;  $P=0.003$ ). The clinical pregnancy rate of study group was significantly higher than that of the control (66.7% vs 55.4%;  $P=0.041$ ). **Conclusion:** Atosiban treatment before embryo transfer may improve pregnancy outcomes of patients in bTET.

**Key words:** oxytocin antagonist; blastcyst; thawed; embryo transfer (ET); pregnancy rate

# 滋阴补阳序贯法联合西药促排卵 对PCOS患者的临床疗效分析

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**【摘要】**目的: 探讨滋阴补阳序贯法联合西药促排卵对PCOS患者的临床疗效。方法: 回顾性分析72例多囊卵巢综合征(PCOS)患者122个促排卵周期患者的临床资料, 所有患者均于促排卵前后使用滋阴补阳中药进行序贯治疗。根据促排卵方案不同分为4组, A组: 克罗米芬(CC) + 促性腺激素释放激素(Gn)( $n=71$ ), B组: 来曲唑(LE) + Gn( $n=30$ ), C组: CC( $n=14$ ), D组: Gn( $n=7$ ), 比较各组间临床和实验室指标。结果: 4组妊娠率比较: C组>A组>B组>D组; Gn用量比较: D组>B组>A组, hCG注射日子宫内膜厚度: A组>D组>B组>C组, 但各指标组间比较均无统计学差异( $P>0.05$ ), 促排天数A组显著高于其它3组( $P<0.05$ )。hCG注射日子宫内膜厚度<7 mm的比例CC组显著高于其它3组( $P<0.05$ )。4组未破裂卵泡黄素化综合征(LUFS)发生率、未启动率均无统计学差异( $P>0.05$ ), 无OHSS发生。按妊娠结局分组比较: bE<sub>2</sub>及bLH水平妊娠组>未孕组, 差异有统计学意义( $P<0.05$ )。妊娠组子宫内膜厚度显著高于未孕组, 各组中A型内膜比例显著高于其它类型内膜。结论: 对PCOS患者选择滋阴补阳序贯法联合CC + Gn促排卵能减少Gn用量, 降低卵巢过度刺激综合征(OHSS)发生率, 增加子宫内膜厚度, 改善子宫内膜容受性, 提高妊娠率。

**关键词:** 滋阴补阳法; 促排卵; 多囊卵巢综合征(PCOS)

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## Effective Analysis of Sequential Method of Nourishing Yin and Tonifying Yang Combined with Controlled Ovarian Induction in Patients with Polycystic Ovary Syndrome

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**【ABSTRACT】 Objective:** To investigate the effect of different therapies with sequential method of nourishing yin and tonifying yang for polycystic ovary on the outcome. **Methods:** A retrospective analysis was performed including 72 patients with polycystic ovary syndrome (PCOS), 122 ovarian induced cycles in total. According to different controlled ovarian hyperstimulation (COH) protocols, they were divided into 4 groups, group A: clomiphene citrate (CC) + gonadotropin (Gn) ( $n=71$ ), group B: letrozole (LE) + Gn ( $n=30$ ), group C: CC ( $n=14$ ), group D: Gn ( $n=7$ ). All patients were treated with sequential method of nourishing yin and tonifying yang during the COH. The clinical and experimental indexes were recorded. **Results:** The pregnancy rate in group C was the highest, group A remained the second. The requirement of Gn in group A was the least. Thickness of endometrium on hCG injection day was the highest in group A, but there was no significant difference among 4 groups. The incidence of endometrial thickness less than 7 mm was highest in group C. There were no significant differences in incidence of luteinized unruptured follicle syndrome (LUFS), cancelled cycle rate in among 4 groups, no ovarian hyperstimulation syndrome (OHSS) occurred in this study. The serum  $E_2$ , LH level, thickness of endometrium were higher in pregnancy group than in non-pregnancy group, differences of the latter two were significant. **Conclusion:** Sequential method of nourishing yin and tonifying yang combined with CC + Gn can reduce dosage of Gn, incidence of OHSS, increase thickness of endometrium, improve endometrial receptivity, thus increasing pregnancy rate.

**Key words:** sequential method of nourishing yin and tonifying yang; controlled ovarian induction; polycystic ovary syndrome (PCOS)

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本研究为江苏省临床医学科技专项-重点病种的规范化诊疗  
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• 循证医学 •

## 激动剂方案中添加重组LH对体外受精-胚胎移植妊娠结局影响的Meta分析

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**【摘要】**目的: 评价激动剂方案中添加重组LH(rLH)的必要性。方法: 计算机检索PubMed、Ovid、EMbase、Medline、Cochrane图书馆等中、外生物医学数据库。收集有关激动剂方案中是否添加rLH的随机对照试验。按Cochrane系统评价方法, 评价所纳入研究的文献质量, 并提取有效数据后采用RevMan5.1软件进行Meta分析。结果: 纳入7个随机对照试验(RCT), 共计1741例患者, 其中FSH+rLH组897例, FSH组844例。Meta分析结果显示: 与FSH组比较, 添加rLH对临床妊娠率( $RR=0.99$ ,  $95\%CI=0.87\sim 1.13$ ,  $P=0.86$ )、活产率( $RR=0.94$ ,  $95\%CI=0.76\sim 1.16$ ,  $P=0.57$ )、种植率( $RR=1.00$ ,  $95\%CI=0.86\sim 1.17$ ,  $P=0.99$ )及流产率( $RR=0.79$ ,  $95\%CI=0.52\sim 1.22$ ,  $P=0.29$ )无影响。但对\*\*\*, 添加rLH降低了获卵数( $WMD=-1.56$ ,  $95\%CI=-1.81\sim -1.32$ ,  $P<0.001$ )及M<sub>II</sub>卵数( $WMD=-1.40$ ,  $95\%CI=-1.79\sim -1.01$ ,  $P<0.001$ )。结论: 与单独应用FSH相比, 添加rLH对临床妊娠率、活产率、种植率及流产率无影响, 但会减少高龄患者获卵数及M<sub>II</sub>卵数。

**关键词:** 添加重组LH(rLH); 激动剂方案; IVF-ET; 随机对照试验(RCT); Meta分析

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## Recombinant LH Supplementation to A GnRH Agonist Protocol in Women Undergoing IVF/ICSI: A Meta-analysis of Randomized Controlled Trials

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**【ABSTRACT】Objective:** To evaluate the effect of recombinant LH (rLH) supplementation to a GnRH agonist protocol. **Methods:** Pubmed, Ovid, EMBASE, MEDLINE, CBM, CNKI, WanFang Data, VIP and Cochrane library were electronically searched. Randomized controlled trials (RCTs) were indentified about rLH supplementation to a GnRH agonist protocol. Study selection and Meta-analysis were conducted according to the Cochrane Handbook for systematic reviews. Data were extracted from these trials by 3 reviewers independently and analyzed by RevMan 5.1 software. **Results:** A total of 7 RCTs involving 1 741 cases were included, of which 897 cases were in FSH+rLH group while the other 844 cases were in FSH group. Meta-analysis indicated that, rLH supplementation had no benefit on the clinical pregnancy rate ( $RR=0.99$ ,  $95\%CI=0.87-1.13$ ,  $P=0.86$ ), live birth rate ( $RR=0.94$ ,  $95\%CI=0.76-1.16$ ,  $P=0.57$ ), implantation rate ( $RR=1.00$ ,  $95\%CI=0.86-1.17$ ,  $P=0.99$ ) and miscarriage rate ( $RR=0.79$ ,  $95\%CI=0.52-1.22$ ,  $P=0.29$ ). However, it can reduce the No. of oocytes retrieved ( $WMD=-1.56$ ,  $95\%CI=-1.81--1.32$ ,  $P<0.001$ ) and metaphase II oocytes ( $WMD=-1.40$ ,  $95\%CI=-1.79--1.01$ ,  $P<0.001$ ) in patients with advanced age. **Conclusion:** Compared with FSH only, rLH supplementation can significantly reduce the No. of oocytes retrieved and metaphase II oocytes in patients with advanced age, and no significant differences between the two groups were found in other indicators.

**Key words:** recombinant LH supplementation; GnRH agonist protocol; IVF-ET; randomized controlled trial (RCT); Meta analysis



• 综述 •

# Notch信号通路在胎盘血管中的作用 及与子痫前期的关系

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**【摘要】** 胎盘血管的发育和重建是胎盘功能、胎儿功能发育的关键, 其异常将直接导致妊娠期并发症如子痫前期, 并最终影响妊娠结局。对人类及其他哺乳动物胎盘的研究表明, Notch信号通路与胎盘血管形成、滋养细胞侵袭等多个过程相关。

**关键词:** 胎盘血管; Notch 信号通路; 子痫前期

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## **Role of Notch Signaling Pathway in Placental Blood Vessels and Its Relationship with Preeclampsia**

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**【ABSTRACT】** The development and remodeling of placental blood vessel determine the function of the placenta, and furthermore intrauterine fetal growth. Placental vascular abnormalities will directly lead to pregnancy complications such as preeclampsia, and ultimately affect pregnancy outcomes. Notch signaling pathway is correlated with formation of the placental blood vessel and the invasiveness of trophoblast.

**Key words:** placental blood vessel; Notch signaling pathway; preeclampsia

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# 输卵管评分在输卵管性不孕症的应用

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**【摘要】** 输卵管性不孕症(TFI)的筛查与诊断对于后续治疗方案及预后起着至关重要的作用。目前临床上常用子宫输卵管碘油造影(HSG)、腹腔镜检查、腹腔镜联合宫腔镜检查等途径评估输卵管情况。输卵管的评估结果对于TFI患者诊治方案的制定具有极大的参考价值,但目前世界上缺乏一致的评分系统,如:Hulka 输卵管评分系统、r-AFS 分期系统、输卵管盆腔病变分度、Hull&Rutherford评估系统、输卵管损害分级、EMs生育指数(EFI)术中探查评分,本研究组也于1990年提出了输卵管评分系统,如此多的评分系统,众说纷纭,各有优劣,尚需更多的研究加以证实。

**关键词:** 输卵管性不孕症(TFI); 输卵管评价; 输卵管评分; 输卵管整形术; 妊娠率(PR)

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## Application of Tubal Scoring in Tubal Factor Infertility

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**【ABSTRACT】** Tubal factor infertility (TFI) is the main reason of increasing infertility rate; therefore, the method used in screening and diagnosis plays a key role in treatment and prognosis. There are many methods to evaluate tubal condition but hysterosalpingography (HSG), laparoscopy, Laparoscopy combined with hysteroscopy are commonly used. Tubal assessments are used as reference of its treatment but since the diversity among experts, the implementation of treatment for TFI is still lack of support.

**Key words:** tubal factor infertility (TFI); tubal assessment; tubal scoring; salpingoplasty; pregnancy rate (PR)

# 辅助生殖技术相关血栓性疾病的防治

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**【摘要】** 辅助生殖技术(ART)并发血栓性疾病的报道逐年增加, 口服避孕药(OCs)、促排卵药物的应用、卵巢过度刺激综合征(OHSS)以及多胎妊娠是血栓性疾病发生的高危因素。在促排卵治疗过程中, 应高度警惕高危人群血栓性疾病的发生, 早期诊断并积极治疗。血栓性疾病的发生重在预防。对于既往有血栓病史或血栓家族史的高危患者必要时可行相关易栓症的遗传性筛查。

**关键词:** 辅助生殖技术(ART); 血栓形成; 预防

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## Prevention of Thrombotic Disease in Assisted Reproductive Technology

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**【ABSTRACT】** Assisted reproductive technology (ART) concurrent thrombotic disease increased year by year, the application of oral contraceptives, ovulation stimulants, ovarian hyperstimulation syndrome (OHSS), and multiple pregnancy are high risk factors of thrombotic diseases. In the process of ovulation induction, we should be on high alert at higher risk of thrombotic diseases, and make early diagnosis and active treatment. Prevention of thrombotic disease was the most important, for patients at high risk of developing a history of blood clots or family history of thrombosis related thrombophilia when necessary and feasible genetic screening.

**Key words:** assisted reproductive technology (ART); thrombosis; prevention

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# 抗苗勒氏管激素在妇产科领域的研究进展

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**【摘要】**抗苗勒氏管激素(AMH)属于转化生长因子 $\beta$ 超家族,在调节生殖细胞发育和分化中发挥重要作用,本文阐述了AMH与卵巢功能、多囊卵巢综合征(PCOS)、辅助生殖以及肿瘤的关系。研究显示血清AMH水平可以准确反映卵巢储备能力,在辅助生殖中具有重要应用价值,AMH还可以作为诊断多PCOS的指标。近年来越来越多的研究表明血清AMH升高是卵巢癌等肿瘤的标志物,且AMH对卵巢癌等肿瘤的生长、迁移和侵袭有抑制作用,可能成为肿瘤治疗的新药物。AMH在妇产科领域具有广阔的应用前景。

**关键词:** 抗苗勒氏管激素(AMH); 卵巢功能; 多囊卵巢综合征(PCOS); 辅助生殖; 肿瘤

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## Research Progress of Anti-Müllerian Hormone in the Field of Gynaecology and Obstetrics

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**【ABSTRACT】** Anti-Müllerian hormone (AMH) belongs to the family of TGF-beta growth factors, and it plays an important role in regulating the development and differentiation of reproduction cells. In this paper we stated the relationship between AMH with ovary function, polycystic ovary syndrome (PCOS), assistant reproduction or tumor. Research indicated that AMH can accurately reflect ovary function, thus it has important practical value in the field of assistant reproduction, AMH also can be used for the marker of dignosing the PCOS. In latest years more and more researches indicated that serum AMH rise can act as the marker of tumor such as ovary cancer. Furthermore, AMH can inhibit growth, migration and invasion of tumor such as ovary cancer, which can be possibly used for the new drug of tumor curity. So AMH has a prosperous application in the field of gynaecology and obstetrics.

**Key words:** anti-Müllerian hormone (AMH); ovary function; polycystic ovary syndrome (PCOS);  
assisted reproduction; tumor



• 临床报道 •

## 静脉用免疫球蛋白对不明原因复发性自然流产患者外周血淋巴细胞和妊娠结局的影响

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**【摘要】**目的: 评估静脉用免疫球蛋白(IVIg)治疗不明原因复发性自然流产(RSA)的效果。方法: 选择既往曾发生 $\geq 3$ 次自然流产的RSA患者65例, 孕早期给予IVIg治疗, 追踪至妊娠结束。检查治疗前、后外周血淋巴细胞亚群, 包括自然杀伤细胞(NK细胞)、毒性T淋巴细胞、辅助性T淋巴细胞和自然杀伤T细胞(NKT细胞)的变化, 进行统计学分析。结果: ①经过IVIg治疗, 外周血NK细胞数量/比例明显下降, 差异有统计学意义( $P < 0.05$ ); ②治疗后, 52例RSA患者成功妊娠并分娩活产, 活产率达88.1%; ③治疗中发生流产的患者外周血NK细胞数量明显高于分娩活产的妇女, 差异有统计学意义( $P < 0.05$ )。结论: IVIg治疗不明原因RSA有比较明确的临床效果, 其机制可能为通过调节患者外周血NK细胞数量/比例而发挥作用。

**关键词:** 静脉用免疫球蛋白(IVIg); 复发性自然流产(RSA); 外周血; 自然杀伤细胞(NK细胞)

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## Effect of Intravenous Immunoglobulin on Peripheral Blood Lymphocyte Cell and Pregnancy Outcome in Women with Recurrent Spontaneous Abortion

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**【ABSTRACT】 Objective:** To evaluate the efficacy of intravenous immunoglobulin (IVIg) in treating the women with recurrent spontaneous abortion (RSA). **Methods:** By flowcytometric analyses, phenotypic changes of a variety of immunological cells were examined including natural killer (NK) cells, cytotoxic T cells, regulatory T cells and NKT cells in peripheral blood of RSA women with IVIg therapy ( $n=65$ ). **Results:** After therapy, 88.1% (52/65) patients had live birth; NK cell percentage significantly decreased after therapy ( $P<0.05$ ). The number and the proportions of NK cells were significantly higher in patients with a subsequent abortion than in those with pregnancy to term. **Conclusion:** IVIg is effective in treating patients with unexplained RSA; IVIg therapy may take an effect through reducing the number and the proportions of peripheral NK cells.

**Key words:** intravenous immunoglobulin (IVIg); recurrent spontaneous abortion (RSA); peripheral blood; natural killer cell (NK cell)

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# 影响冻融胚胎移植妊娠结局的相关因素分析

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**【摘要】** 目的: 探讨影响冻融胚胎移植(FET)妊娠结局的相关因素。方法: 回顾性分析 324 个周期行 FET 患者的临床资料, 分析患者年龄、体质量指数(BMI)、移植日子宫内膜厚度、内膜准备方案、移植胚胎数等相关因素对 FET 妊娠结局的影响。结果: 324 个周期共解冻胚胎 727 个, 复苏成活 720 个(99.0%), 临床妊娠 144 例(44.4%), 胚胎植入 196 例(27.2%)。其中自然内膜准备周期组和激素替代内膜准备周期组患者年龄、不孕年限、基础卵泡刺激素(bFSH)、基础黄体生成素(bLH)、基础雌二醇(bE<sub>2</sub>)、复苏胚胎数、移植胚胎数、移植日子宫内膜厚度、胚胎种植率及临床妊娠率组间均无统计学差异( $P>0.05$ )。年龄 $\leq 35$ 岁组的临床妊娠率高于年龄 $>35$ 岁组, 差异有统计学意义( $P<0.05$ ); BMI $\geq 24.0$  kg/m<sup>2</sup>的肥胖组临床妊娠率与正常体质量(BMI=18.5~23.9 kg/m<sup>2</sup>)组无统计学差异( $P>0.05$ ); 移植日子宫内膜厚度 $\geq 7$  mm组的临床妊娠率高于移植日子宫内膜厚度 $<7$  mm组, 但差异无统计学意义( $P>0.05$ ); 各移植胚胎数组间临床妊娠率无统计学差异( $P>0.05$ )。结论: 年龄是影响 FET 临床结局的重要因素, 内膜准备方案、BMI、移植日内膜厚度、移植胚胎数对冻融胚胎移植临床结局无影响。

**关键词:** 冻融胚胎移植(FET); 自然周期; 激素替代周期; 临床妊娠率

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## Influence of Related Factors on the Pregnancy Outcome of Frozen-thawed Embryo Transfer

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**【ABSTRACT】 Objective:** To investigate the influence of related factors on the pregnancy outcome of frozen-thawed embryo transfer (FET). **Methods:** The clinical data of 324 cycles of FET were retrospectively analyzed. Patients' age, body mass index (BMI), endometrial thickness on the day of transplantation, endometrial preparation protocol, the number of embryo transferred were compared. **Results:** A total of 727 embryos were thawed in 324 transfer cycles, 720 (99.0%) resuscitated, 144 cases of clinical pregnancy (44.4%), embryo implantation in 196 cases (27.2%). There were no obvious differences in the patients' age, infertility duration, basal follicle stimulating hormone (FSH), basal luteinizing hormone (bLH), basal estradiol (bE<sub>2</sub>), embryos resuscitated, embryos transferred, endometrial thickness on the day of transplantation, embryos implantation rate, clinical pregnancy rate between nature cycle and hormone replacement cycle ( $P>0.05$ ). Clinical pregnancy rate of patients who were less than 35 years old were higher than that of the older than 35 years old, the difference was statistically significant ( $P<0.05$ ). The difference was not statistically significant in implantation rates and clinical pregnancy rates between the obesity group and the normal weight group ( $P>0.05$ ). Clinical pregnancy rate of endometrial thickness  $\geq 7$  mm on the day of transplantation was higher than that of endometrial thickness  $<7$  mm on the day of transplantation, but the difference was not statistically significant ( $P>0.05$ ); the difference was not statistically significant between transferred 3 embryos and transferred 2 embryos. **Conclusion:** The patients' age is an important affecting factor on the outcome of FET, but endometrial preparation protocols, BMI, endometrial thickness on the day of transplantation, the number of embryos transferred did not affect the clinical outcome.

**Key words:** frozen-thawed embryo transfer (FET); nature cycle; hormone replacement cycle; clinical pregnancy rate

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# 冻融胚胎移植周期中卵裂期胚胎 移植策略初步探讨

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**【摘要】**目的: 探讨第3日冻融胚胎合适的移植策略。方法: 收集在本院行卵裂期(第3日)冷冻胚胎移植(FET)的3 694个周期的患者资料进行回顾性分析, 根据移植胚胎数将患者分为移植1枚胚胎组(A组)、2枚胚胎组(B组)和3枚胚胎组(C组)。依据患者年龄分别再分为不同的年龄组(1组 <35岁、2组 35~39岁、3组  $\geq 40$ 岁); 另根据胚胎质量分优质胚胎组和非优质胚胎组。结果: A、B、C组临床妊娠率分别为23.03%、43.95%、40.18%, A组与B组间及A组与C组间比较, 均有统计学差异( $P < 0.01$ )。A1、A2、A3 3组的临床妊娠率分别为28.34%、18.84%、8.33%, A1与A3组间有统计学差异( $P < 0.01$ ); B1、B2、B3 3组的临床妊娠率分别为48.13%、34.50%、15.23%, 各組间两两比较均有统计学差异( $P < 0.01$ ); C1、C2、C3 3组的临床妊娠率分别为45.24%、36.63%、16.67%, C1与C3组间以及C2与C3组间比较, 均有统计学差异( $P < 0.01$ ,  $P < 0.05$ )。临床妊娠率在A、B、C组 $\geq 40$ 岁亚间均无统计学差异( $P > 0.05$ )。A、B、C组中移植优质胚胎者的临床妊娠率显著高于非优质胚胎者( $P < 0.01$ )。结论: 第3日FET周期中, 应依据患者年龄和胚胎质量对不同患者制定个体化的移植方案。选择性单囊胚移植是今后的努力方向。

**关键词:** 冻融胚胎移植(FET); 卵裂期(第3日)胚胎; 单胚胎移植; 临床妊娠率; 多胎妊娠率

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## Study of Cleavage Stage (Day 3) Embryo Transfer Strategy in Frozen-thawed Embryo Transfer Cycle

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**【ABSTRACT】 Objective:** To explore suitable embryo transfer strategy in frozen-thawed embryo transfer (FET) cycle. **Methods:** A retrospective analysis was performed on 3 694 cycles of cleavage stage (day 3) embryo transfer. The patients were divided into 3 groups according to the number of embryos transferred, 1 embryo (group A), 2 embryos (group B) and 3 embryos (group C). Groups A, B and C were divided into different subgroups according to patients' age and quality of embryos: <35 years (groups A1, B1 and C1), 35–39 years (group A2, B2 and C2),  $\geq 40$  years (groups A3, B3 and C3) and high-quality embryo subgroups, low-quality embryo subgroups. **Results:** A total of 3 694 thawing cycles involving day 3 embryos were analyzed. Clinical pregnancy rates of groups A, B and C were 23.03%, 43.95%, 40.18%, respectively. There were significantly statistic differences among groups A, B ( $P < 0.01$ ) and groups A, C ( $P < 0.01$ ). The pregnancy rates of A1, A2, A3, B1, B2, B3 and C1, C2, C3 were 28.34%, 18.84%, 8.33%, 48.13%, 34.50%, 15.23%, and 45.24%, 36.63%, 16.67%, respectively. There were significantly statistic differences among groups B1, B2, B3 ( $P < 0.01$ ) and groups C1, C3 and groups C2, C3 ( $P < 0.01$ ,  $P < 0.05$ ). There were no significantly statistic differences among groups A, B, C in  $\geq 40$  years patients. There were significantly statistic differences among high-quality embryo groups and low-quality embryo groups. **Conclusion:** We should draw up individual embryo transfer strategy depending on patient's age, the number and the quality of embryos transferred in day 3 FET cycles. Elective single embryo transfer will be our future struggle direction.

**Key words:** frozen-thawed embryo transfer (FET); cleavage stage (day 3) embryos; single embryo transfer; clinical pregnancy rate; multiple pregnancy rate

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# 肌壁间子宫肌瘤对体外受精-胚胎移植 临床结局的影响

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**【摘要】** 目的: 探讨宫腔形态无改变的肌壁间子宫肌瘤对体外受精/卵胞质内单精子注射-胚胎移植(*in vitro* fertilization/intracytoplasmic sperm injection-embryo transfer, IVF/ICSI-ET)临床结局的影响。方法: 选择行IVF/ICSI-ET治疗伴单发或多发肌壁间子宫肌瘤且宫腔形态正常的93例不孕症患者作为研究对象, 共行胚胎移植104个周期(研究组); 按对照组与研究组1:3比例随机抽取同期行IVF/ICSI-ET且无子宫肌瘤的308例患者作为对照组, 共行IVF/ICSI-ET周期312个, 分析控制性超促排卵(COH)、体外受精参数和妊娠结局。结果: 研究组患者的年龄、不孕年限显著高于对照组( $P<0.05$ ), 促性腺激素(Gn)使用天数、获卵数显著低于对照组( $P<0.05$ ); 体质指数(BMI)、Gn用量、双原核(2PN)率、卵裂率、优质胚胎率、临床妊娠率、着床率、异位妊娠率、早期流产率、晚期流产率、活产率、单胎活产率、双胎活产率、早产率、低体重儿率、出生缺陷率组间均无统计学差异( $P>0.05$ )。结论: 宫腔形态无改变的肌壁间子宫肌瘤对IVF-ET的临床结局无明显不良影响。

**关键词:** 肌壁间子宫肌瘤; 体外受精(IVF); 妊娠结局

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## Impact of Intramural Fibroids with Normal Uterine Cavity on the Outcomes of IVF/ICSI-ET

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**【ABSTRACT】 Objective:** To investigate whether intramural fibroids with normal uterine cavity have an adverse effect on the outcomes of *in vitro* fertilization/intracytoplasmic sperm injection-embryo transfer (IVF/ICSI-ET). **Methods:** The data of 102 IVF/ICSI-ET cycles out of 93 women with intramural fibroids were analyzed retrospectively (research group), and homeochronous 312 IVF/ICSI-ET cycles out of 308 women without intramural fibroids were randomly chosen according to the ratio of 1 : 3 to research group and served as control group. The patients' characteristics, IVF/ICSI parameters and pregnancy outcomes were compared between the two groups. **Results:** The patients' age, duration of infertility in research group were significantly higher than those in control group ( $P < 0.05$ ), but the duration of gonadotropin (Gn) administration and the No. of oocytes retrieved were significantly lower than those in control group ( $P < 0.05$ ). There was no significant difference in body mass index (BMI), dosage of Gn administration, 2PN rate, cleavage rate, high-quality embryo rate, clinical pregnancy rate, implantation rate, ectopic pregnancy rate, early abortion rate, late abortion rate, live birth rate, single birth rate, twins live birth rate, premature delivery rate, infant of low-birth weight rate and birth defects rate ( $P > 0.05$ ) between the two groups. **Conclusion:** Intramural fibroids with normal uterine cavity have no adverse effect on IVF outcomes.

**Key words:** intramural fibroid; *in vitro* fertilization/intracytoplasmic sperm injection-embryo transfer (IVF/ICSI-ET); pregnancy outcome



# 不育男性精浆左旋肉碱浓度 与精子活力和浓度的关系

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**【摘要】**目的: 探讨精浆左旋肉碱测定在男性不育症诊疗中的临床意义。方法: 按照第5版《世界卫生组织人类精液检查与处理实验室手册》的参考值, 将不育男性按照精液常规分析结果分为精子活力正常组(前向运动精子百分率 $\geq 32\%$ )( $n=283$ )和弱精子症组(前向运动精子百分率 $< 32\%$ )( $n=892$ )。通过比色法检测精浆中的游离左旋肉碱含量, 分析左旋肉碱浓度与精子活力、精液浓度的相关性。通过受试者操作特征分析曲线(receiver operating characteristic curve, ROC curve)确定左旋肉碱浓度的阈值, 以阈值为分界点, 将弱精子症患者分为高于左旋肉碱阈值组和低于左旋肉碱阈值组, 分析左旋肉碱与精子活力和精子浓度的相关性。结果: 弱精子症组的精浆左旋肉碱浓度( $384.14 \pm 188.81 \mu\text{mol/L}$ )显著低于精子活力正常组( $434.04 \pm 171.77 \mu\text{mol/L}$ ,  $P < 0.05$ )。精子活力正常组和弱精子症组精浆中的左旋肉碱含量与前向运动精子百分率和精子浓度的相关性极低或不相关( $r < 0.2$ )。肉毒碱检测的ROC曲线下面积(AUC)为0.592, 阈值为380.9, 低于左旋肉碱阈值弱精子症组与前向运动精子百分率有较弱的正相关关系( $r=0.329$ ,  $P=0.000$ )。结论: 对于拟行辅助生育的不育男性患者, 精浆中左旋肉碱浓度作为精浆生化的指标之一, 可能对弱精子症患者有一定的临床参考意义。

**关键词:** 左旋肉碱; 弱精子症; 辅助生育

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## Correlation between L-carnitine Level of Semen Plasma and Sperm Motility As Well As Sperm Concentration in Infertile Male Patients

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**【ABSTRACT】 Objective:** To investigate the clinical meaning of the L-carnitine level in semen plasma. **Methods:** The infertile male patients were divided into two groups according to “WHO laboratory manual for the examination and process of human semen (the fifth edition)”, 283 cases in the normal sperm motility group (progressive motility  $\geq 32\%$ ) and 892 cases in asthenozoospermia group (progressive motility  $< 32\%$ ). The carnitine level in semen plasma, the correlation between the carnitine level and sperm motility as well as sperm concentration of the two groups were compared. The receiver operating characteristic (ROC) curve were analyzed to determine the cut-off value of L-carnitine, dividing the asthenozoospermia group into two subgroups by the cut-off value, the correlation between the carnitine level and sperm motility as well as sperm concentration of the two subgroups were further analyzed. **Results:** Carnitine level of asthenozoospermia group ( $384.14 \pm 188.81 \mu\text{mol/L}$ ) was significantly lower than that in the normal sperm motility group ( $434.04 \pm 171.77 \mu\text{mol/L}$ ,  $P < 0.05$ ). There was no correlation between the carnitine level and the percentage of sperm with progressive motility as well as sperm concentration in the two groups. The area under the ROC curve was 0.592, cut-off value was 380.9, there was a weak positive correlation between the carnitine level and the percentage of sperm with progressive motility in the lower cut-off subgroup of asthenozoospermia ( $r = 0.329$ ,  $P = 0.000$ ). **Conclusion:** For the infertile male population who resort to assisted reproduction technique, the carnitine level may be one of the influencing factors for the asthenozoospermia.

**Key words:** L-carnitine; asthenozoospermia; assisted reproduction

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• 个案报道 •

# 单角子宫IVF-ET助孕双胎妊娠分娩: 1例病例报道

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**【摘要】**目的: 报道1例单角子宫患者行IVF-ET助孕双胎妊娠成功分娩活产的病案。方法: 对本院接受IVF-ET助孕的1例原发性不孕单角子宫患者进行回顾性总结与分析。结果: 采用GnRHa长方案控制性超促排卵(COH), 获优质胚胎13枚, 移植8c II级胚胎2枚, 宫内双胎妊娠因严重子痫前期于34<sup>+3</sup>周行剖宫产, 早产2名健康活婴。结论: 对子宫肌层厚度及宫腔容积正常的单角子宫不孕患者行IVF-ET助孕治疗是可行的。但应尽量避免多胎妊娠, 减少流产、早产等并发症的发生, 争取良好的妊娠结局。

**关键词:** 子宫畸形; 体外受精 - 胚胎移植(IVF-ET); 单角子宫

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## Unicornuate Uterus in Twin Pregnancy by IVF-ET: A Case Report

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**【ABSTRACT】 Objective:** To report a case of unicornuate uterus in twin pregnancies by IVF-ET. **Methods:** A retrospective clinical study was performed to analyze a case of unicornuate uterus in twin pregnancies by IVF-ET. **Results:** The infertile patient underwent controlled ovarian hyperstimulation (COH) by conventional GnRH $\alpha$  protocol. Thirteen high-quality embryos were obtained, 2 embryos of 8-cell level II were implanted to intrauterine. The infertile patient with unicornuate uterus got twin pregnancy and gave birth to 2 premature babies by pregnancy cesarean. **Conclusion:** It is feasible to perform IVF-ET on infertile patients with unicornuate uterus of normal myometrium thickness. For lower the risks of abortion and premature delivery and everything to strive for good pregnancy outcome, we should avoid multiple pregnancy as far as possible.

**Key words:** uterine malformation; *in vitro* fertilization and embryo transfer (IVF-ET); unicornuate uterus