

• 实验研究 •

睾酮对胰岛素诱导的肝细胞糖原合成和 Akt/GSK3 β 磷酸化水平的影响

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【摘要】目的: 探讨睾酮(T)在肝脏胰岛素抵抗(IR)形成过程中的作用及其分子途径。方法: 将成年 C57BL/6 雌鼠随机分为 T 组($n=11$)及对照组($n=10$), T 组小鼠每日腹腔注射 T ($10 \mu\text{g/g}$ 体质量, 溶剂为蓖麻油), 对照组每日腹腔注射相同体积的蓖麻油, 连续给药 24 周后处死, 分离出原代小鼠肝细胞进行体外培养, 用胰岛素(Ins)处理细胞后, 通过液闪法检测原代肝细胞中的糖原合成率。分别用 10^{-5} mol/L 和 10^{-7} mol/L 浓度的 T 溶液短时间(1 h)或长时间(36 h)处理体外培养的人肝癌细胞系 BEL-7404 后, 再用 Ins 处理 BEL-7404 细胞, 然后通过液闪法检测细胞中的糖原合成率; 并通过免疫印迹法检测细胞中 Akt、GSK3 β 蛋白的表达水平和磷酸化水平。结果: Ins 对 T 组小鼠原代肝细胞中糖原合成的诱导作用显著低于对照组($P<0.05$), 提示 T 组小鼠原代肝细胞对 Ins 的敏感性降低。BEL-7404 细胞经 T 短时间(1 h)处理后, Ins 对细胞中糖原合成率以及 Akt 和 GSK3 β 蛋白活性的诱导作用显著提高($P<0.05$); 但当 BEL-7404 细胞经高浓度 T (10^{-5} mol/L)长时间(36 h)处理后, Ins 对细胞中糖原合成率以及 Akt 和 GSK3 β 蛋白活性的诱导作用显著降低($P<0.05$), 提示高浓度 T 在短时间内能增强 BEL-7404 细胞对 Ins 的敏感性, 但长时间暴露后会降低细胞对 Ins 的敏感性。结论: 长时间的 T 暴露可能会降低肝细胞中 Ins 信号转导活性, 从而干扰肝细胞对 Ins 的敏感性, 导致 IR 的产生。

关键词: 睾酮(T); 肝细胞; 糖原合成; 胰岛素信号途径; 胰岛素抵抗(IR)

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• 实验研究 •

Effect of testosterone on the rate of glycogen synthesis and the activity of Akt and GSK3 β proteins stimulated by insulin in hepatocytes

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【ABSTRACT】 Objective: To investigate the role of testosterone (T) in the formation of insulin resistance (IR) in liver and its molecular pathway. **Methods:** Adult C57BL/6 female mice were randomly divided into T group ($n=11$) and control group ($n=10$). Mice in T group were daily intraperitoneal injected with T (1 mg T/100 g body weight, dissolved in castor oil), mice in control group were treated with intraperitoneal injection of the same volume of castor oil. After 24 weeks, the mice were killed, and primary mice hepatocytes were isolated and cultured *in vitro*. After treatment of cells with insulin (Ins), the rate of glycogen synthesis in primary hepatocytes was detected by a liquid scintillation method. The *in vitro* culture of human hepatocellular carcinoma cell line BEL-7404 were pretreated with 10^{-5} mol/L and 10^{-7} mol/L concentration of T solution in short time (1 h) or long time (36 h) respectively, then treated by Ins, the rate of glycogen synthesis of the BEL-7404 cells were detected by a liquid scintillation method. The expression and phosphorylation levels of GSK3 β and Akt proteins were detected by Western blotting. **Results:** The inducing effect of Ins on glycogen synthesis in primary hepatocytes of mice in T group was significantly lower than that in control group ($P<0.05$), suggesting that the sensitivity of primary hepatic cells to Ins decreased in T group. BEL-7404 cells were pretreated by T in short time (1 h) then the treated by Ins, the glycogen synthesis rate, as well as Akt and GSK3 β proteins activity were significantly increased ($P<0.05$). But when BEL-7404 cells were pretreated with high concentration (10^{-5} mol/L) T for a long time (36 h), the rate of glycogen synthesis induced by Ins and the activity of Akt and GSK3 β proteins were decreased significantly ($P<0.05$), which suggested that high concentration T can increase the sensitivity of BEL-7404 cells to Ins in a short time, but decrease the sensitivity to Ins in a prolonged exposure. **Conclusion:** T in a long time exposure may reduce insulin signaling activity in liver cells, which leads to IR.

Key words: testosterone (T); hepatocytes; glycogen synthesis; insulin signaling pathway; insulin resistance (IR)

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正常妊娠滋养层组织中Lin28B表达变化的研究

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【摘要】目的: 探讨Lin28B在正常妊娠不同阶段滋养层细胞中的表达变化及其临床意义。方法: 收集40例正常早期妊娠者(孕早期组), 包括20例妊娠5~7⁺6周(孕早A组)和20例妊娠8~12⁺2周(孕早B组), 15例孕17~27周(孕中期组), 以及20例孕37~41周(孕晚期组), 共75例正常孕妇的绒毛和胎盘组织。采用RT-qPCR、Western blotting和免疫组织化学方法检测胎盘组织Lin28B基因和蛋白的表达差异及细胞定位。结果: ①在正常妊娠不同时期的滋养层组织中细胞滋养细胞和合体滋养细胞中均可检测到Lin28B蛋白的表达。②Lin28B mRNA表达量各组间有统计学差异($P < 0.05$), 孕早A组最高, 随着孕周进展逐渐下降, 至孕晚期达最低水平。③正常妊娠不同时期的滋养层组织中Lin28B蛋白表达呈现为随着孕周的增加而逐渐下降趋势。结论: Lin28B在正常妊娠进展过程中表达下调, 提示其可能参与了滋养细胞的增殖和浸润及胎盘的发育。

关键词: Lin28B; 正常妊娠; 绒毛; 胎盘; 滋养细胞

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Expression and significance of Lin28B in trophoblast tissue of normal pregnancy

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【ABSTRACT】 Objective: To investigate the expression and clinical significance of Lin28B in different stages of normal pregnancy trophoblast cells. **Methods:** Totally 75 cases of normal villi and placenta of pregnant women were collected, including 40 cases of early pregnancy (early pregnancy group) which consists of 20 cases of 5-7⁺⁶-week gestation (early pregnancy group A) and 20 cases of 8-12⁺²-week gestation (early pregnancy group B), 15 cases of the second trimester pregnancy (middle pregnancy group) and 20 normal late pregnancy (late pregnancy group). The expression and localization of Lin28B mRNA and protein in placenta were evaluated by RT-qPCR, Western blotting and immunohistochemistry. **Results:** 1) Lin28B was positively expressed in the villi and placenta of all groups. 2) Lin28B mRNA expression in each group was significantly different ($P<0.05$), the highest was in the early pregnancy group A and was decreased to the lowest level in the third trimester along with the progression of gestational age ($P<0.05$). 3) The expression of Lin28B in different stages of normal pregnancy trophoblast cells decreased gradually along with the progression of gestational age ($P<0.05$). **Conclusion:** The expressions of Lin28B in normal pregnancy progression presented down-regulated, suggesting that it might be involved in proliferation and infiltration functions of trophoblast cells and the development of the placenta.

Key words: Lin28B; normal pregnancy; villus; placenta; trophoblast cells

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多次退火环状循环扩增和多重置换扩增技术在β地中海贫血基因变异诊断效率中的差异分析

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【摘要】目的: 探讨最适的β地中海贫血疾病*HBB*基因单细胞全基因组扩增方法。方法: 60份β地中海贫血成纤维细胞(*HBB*基因变异位点CD17和IVS II 654)和48份废弃胚胎单个卵裂球进行多次退火环状循环扩增法(MALBAC)和多重置换扩增法(MDA)扩增及高通量测序, 比较位点检测率、等位基因脱扣(ADO)率及扩增均一度等。结果: β地中海贫血疾病*HBB*基因MALBAC技术位点检测率(100%)高于MDA技术(96.3%); CD17和IVS II 654的ADO率MALBAC技术为9.09%和0.00%, MDA技术为23.08%和19.23%; 对编码人β-珠蛋白的*HBB*基因附近60个SNP位点检测显示MALBAC技术ADO率为12.04%, MDA技术为21.25%; MALBAC技术拷贝数变异检测变异系数为0.13, MDA技术为0.15。结论: β地中海贫血单细胞诊断MALBAC法优于MDA法。

关键词: 多次退火环状循环扩增法(MALBAC); 多重置换扩增法(MDA); 植入前遗传学诊断(PGD); β地中海贫血; 等位基因脱扣(ADO)率

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Comparison of multiple annealing and looping-based amplification cycles (MALBAC) and multiple displacement amplification (MDA) in variation diagnosis of β -thalassemia disease at single-cell level

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【ABSTRACT】 Objective: To detect the application efficacy on β -thalassemia of multiple annealing and looping-based amplification cycles (MALBAC). **Methods:** Totally 60 fibroblasts samples with variation of CD17 and IVS II 654 were amplified at single-cell level by MALBAC and multiple displacement amplification (MDA), respectively. Totally 48 single-blastomere derived from discarded embryos, were amplified by MALBAC and MDA. Re-sequencing with high depth was performed to detect difference of genome coverage, uniformity, allele drop out (ADO) rates between two methods. **Results:** The success rate of *HBB* gene amplification with fibroblasts samples was 100.00% in MALBAC and 96.29% in MDA. ADO rate for CD17 allelic was 9.09% in MALBAC and 23.08% in MDA. ADO rate for IVS II 654 allelic was 0.00% in MALBAC and 19.23% in MDA. ADO rate for 60 SNP markers close to the *HBB* gene was 12.04% in MALBAC and 21.25% in MDA. The coefficient of variation (CV) of copy number variation (CNV) at single-cell level detection in MALBAC and MDA was 0.13 and 0.15, respectively. **Conclusion:** MALBAC has a higher level of uniformity, specificity and lower ADO rate in pre-implantation genetic diagnosis (PGD) for β -thalassemia at single-cell level than that of MDA. Combined with haplotype analysis with SNP markers, MALBAC is superior to MDA in PGD of β -thalassemia disease.

Key words: multiple annealing and looping-based amplification cycles (MALBAC); multiple displacement amplification (MDA); pre-implantation genetic diagnosis (PGD); β -thalassemia; allele drop out (ADO)

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· 临床研究 ·

自然周期准备内膜在子宫内膜异位症患者 冻融胚胎移植中的结局分析

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【摘要】目的: 研究以自然周期作为子宫内膜准备方式对子宫内膜异位症(EMS)患者冻融胚胎移植(FET)妊娠结局的影响。方法: 回顾性分析EMS患者353个FET周期, 按EMS严重程度分组, A组: I~II期, 120个周期; B组: III~IV期, 233个周期; 另将B组中囊肿复发的47个周期设为D组; 而将输卵管因素不孕患者的300个FET周期纳入为对照组(C组), 比较A、B、C组患者自然周期准备内膜的妊娠结局。结果: A、B、C组患者的种植率、活产率、继续妊娠率、流产率、妊娠期并发症率无统计学差异($P>0.05$), 且妊娠结局与EMS的分期无关。A、B、C组均没有出生缺陷儿。当高质量的胚胎移植时, 卵巢内膜异位囊肿并不影响妊娠结局。B组较C组低出生体质量儿和早产儿的发生率高。结论: EMS患者自然周期准备内膜与输卵管性因素不孕患者有相似的妊娠结局, 且与EMS严重程度无关, 妊娠结局不受内膜异位囊肿的影响, 是经济、高效的内膜准备方法。

关键词: 冻融胚胎移植(FET); 自然周期; 子宫内膜异位症(EMS); 临床妊娠结局; 激素替代

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• 临床研究 •

Efficacy of natural cycle endometrial preparation for frozen-thawed embryo transfer in patients with endometriosis

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【ABSTRACT】 Objective: To study the efficacy of natural cycle (NC) endometrial preparation for frozen-thawed embryo transfer (FET) in women with endometriosis (EMS). **Methods:** A retrospective study was carried out in women with EMS, including 120 cycles with stage I–II EMS (group A); 233 cycles with stage III–IV EMS (group B); 300 cycles with tubal factor infertility (group C). In group B, 42 patients received 47 cycles and had endometrial cyst recurrence (group D) after laparoscopic treatment. All groups were prepared for FET using a NC protocol. **Results:** The implantation rate (group A: 32.4%, group B: 36.0%, group C: 30.4%, $P=0.169$), the pregnancy rate (group A: 43.3%, group B: 50.2%, group C: 45.3%, $P=0.381$), and the live-birth rate (group A: 35.83%, group B: 39.91%, group C: 39.0%, $P=0.587$) were similar. No differences were observed in ongoing pregnancy rate, miscarriage rate, and pregnancy complication rate, independently from severity of EMS. No congenital birth defects were found. When high-quality embryos were transferred, pregnancy outcomes were not affected by active endometrial cyst. **Conclusion:** There was no difference in pregnancy outcomes between EMS patients received NC endometrial preparation and patients with tubal infertility, which were not affected by the stage of EMS. The pregnancy outcomes were not affected by active endometrial cyst.

Key words: frozen-thawed embryo transfer (FET); natural cycle (NC); endometriosis (EMS); clinical pregnancy outcomes; hormone replacement

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探讨辅助孵化在既往种植失败患者 解冻周期中的合理化应用

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【摘要】目的: 探讨在既往胚胎种植失败患者的解冻周期中如何合理化应用辅助孵化(AH)。方法: 本研究共纳入了579名既往种植失败的患者, 其中242例行激光AH(LAH组), 337例未行AH(对照组)。比较组间临床妊娠率、种植率及活产率等; 另根据患者的年龄、既往移植次数、胚胎评分及移植胚胎受精方式再进行分组, 比较不同组别的妊娠结局。结果: 妊娠率、种植率及活产率在LAH组与对照组组间无统计学差异($P>0.05$), 但分组分析结果显示, 既往移植次数 >2 次的患者以及移植卵泡质内单精子显微注射(ICSI)胚胎的患者, LAH能显著提高活产率(25.5% vs 5.3%; 37.0% vs 23.9%, $P<0.05$)。结论: LAH并不适合作为解冻胚胎移植的常规移植策略, 但对于既往移植次数 >2 次的未孕者及移植ICSI胚胎的患者, LAH能明显改善妊娠结局。

关键词: 辅助孵化(AH); 解冻周期; 既往种植失败

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To explore the proper applications of assisted hatching in the frozen-thawed cycles for patients with previous embryo implantation failure

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【ABSTRACT】 Objective: To investigate the proper applications of assisted hatching (AH) in frozen-thawed cycles for patients with previous embryo implantation failure. **Methods:** A total of 579 patients with previous embryo implantation failure in frozen-thawed cycles were included, 242 of which were treated by laser AH (LAH group) while the remainings were non-LAH treated (control group). The clinical pregnancy rate, the implantation rate and the live-birth rate were compared between the two groups. A sub-grouping analysis was further carried out according to the age, previous transplanting times, embryo grade as well as the fertilization method of transplanted embryo, the pregnancy outcome among sub-groups was also compared. **Results:** There were no statistic differences of the clinical pregnancy rate, the implantation rate and the live-birth rate between LAH group and control group. However, sub-grouping analysis indicated that the patients who received more than 2 times of transplantation and intracytoplasmic sperm injection (ICSI) embryos transplantation, the live-birth rate of LAH group was significantly higher than that in control group (25.5% vs 5.3%; 37.0% vs 23.9%, $P < 0.05$). **Conclusion:** The LAH is not fit for frozen-thawed cycles as a common transplanting protocol, but for the patients who received transplantation more than 2 times and transplanting ICSI embryos, LAH can definitely improve the live-birth rate.

Key words: assisted hatching (AH); frozen-thawed cycle; previous embryo implantation failure

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三维超声参数对IVF/ICSI-ET妊娠结局的预测价值

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【摘要】目的: 探讨三维超声参数对体外受精/卵胞质内单精子显微注射-胚胎移植(IVF/ICSI-ET)妊娠结局的预测价值。方法: 回顾性分析697例行IVF/ICSI助孕患者hCG注射日子宫内膜及内膜下超声参数, 根据临床妊娠与否分组, 比较妊娠组与非妊娠组的资料, 并进一步根据促排卵方案行分层分析, 研究各项超声参数与妊娠结局的关联。结果: ①妊娠组的年龄、不孕年限和IVF周期数显著低于非妊娠组($P<0.05$), 而妊娠组的子宫内膜厚度、内膜体积大于非妊娠组($P<0.05$), 妊娠组螺旋动脉收缩期速度(PSV)和舒张末期速度(EDV)、内膜下1 mm血流指数(FI)、内膜下3 mm的FI和血管血流指数(VFI)高于非妊娠组, 差异均有统计学意义($P<0.05$)。②超声参数与长方案患者妊娠结局无明显关联, 而在短方案促排卵患者中, 妊娠组和非妊娠组的内膜厚度及螺旋动脉EDV存在统计学差异($P<0.05$)。③Logistic回归显示周期数和内膜厚度可作为短方案患者妊娠结局的预测指标, 受试者工作特征(ROC)曲线分析也提示内膜厚度对妊娠具有一定的预测价值。结论: IVF/ICSI患者hCG注射日子宫内膜和内膜下三维超声参数对妊娠结局的预测价值十分有限, 内膜厚度对短方案患者妊娠具有一定的预测作用。

关键词: 体外受精/卵胞质内单精子显微注射-胚胎移植(IVF/ICSI-ET); 超声; 三维能量多普勒; 子宫内膜容受性

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Effect of three-dimensional ultrasound on the prediction of pregnancy outcome during IVF/ICSI-ET

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【ABSTRACT】 Objective: To investigate the prediction value of parameters by three-dimensional ultrasound on pregnancy outcome during *in vitro* fertilization/intracytoplasmic sperm injection-embryo transfer (IVF/ICSI-ET). **Methods:** Ultrasound parameters of 697 patients measured on hCG injection day were retrospectively analyzed. These variables were compared between pregnant and non-pregnant patients. Stratified analysis was then conducted according to the controlled ovarian hyperstimulation (COH) protocol. **Results:** Compared with non-pregnant patients, pregnant women exhibited significantly lower age, infertility duration, IVF cycle and higher endometrial thickness, endometrial volume, endometrial spiral arteries peak systolic velocity (PSV), end diastolic velocity (EDV), subendometrial flow index (FI) and vascular flow index (VFI). There were significant differences in endometrial thickness and EDV between pregnant and non-pregnant women who were treated with short protocol. Logistic analysis showed that IVF cycle and endometrial thickness could predict the pregnancy outcome of patients treated with short protocol. Receiver operating characteristic (ROC) curve analysis was also conducted to evaluate the predictive value of endometrial thickness on pregnancy outcome. **Conclusion:** Three-dimensional ultrasound measurement on hCG injection day does not play an important role in the prediction of pregnancy outcome during IVF/ICSI-ET, while endometrial thickness correlates with pregnancy outcome of patients treated with short protocol.

Key words: *in vitro* fertilization/intracytoplasmic sperm injection-embryo transfer (IVF/ICSI-ET); ultrasound; three-dimensional Doppler; endometrial receptivity

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移植无原核胚胎出生健康子代

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【摘要】目的: 观察无原核(PN)胚胎的发生率、影响因素及移植OPN胚胎周期的临床治疗结局。方法: 回顾性分析4 424个IVF-ET周期移植OPN来源胚胎的结局。结果: OPN胚胎的发生率为11.3%。女方的年龄、获卵数及优质胚胎率与OPN的发生率相关。70个周期移植了112个OPN来源的卵裂期胚胎, 获得的临床妊娠率为24.3% (17/70), 植入率为17.0% (19/112), 流产率为11.8% (2/17)。1例死产。13个周期活产13个健康子代, 未见畸形的发生。对OPN来源的囊胚进行复苏周期移植, 可获得与2PN囊胚相似的临床妊娠率及植入率, 但流产率较高, 差异有统计学意义。结论: IVF周期中, 含有OPN优质胚胎的周期可能有较好的临床治疗结局。形态正常的OPN胚胎有较好的胚胎发育潜能, 在无2PN胚胎的情况下, 可考虑移植OPN来源胚胎。

关键词: 异常受精; 原核(PN); 妊娠

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Live births resulting from “unfertilized” embryos

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【ABSTRACT】 Objective: To investigate the incidence and influence factors of embryos derived from “unfertilized oocytes”, i.e. oocytes do not displaying pronuclei (PN) at the time of the fertilization check, and the clinical pregnancy outcomes when transferring OPN embryos. **Methods:** In this retrospective study, 4 424 IVF-ET cycles were reviewed and the outcome of transferring OPN embryos was analyzed. **Results:** The occurrence rate of OPN embryos was 11.3% (4 966/43 949). The female age, the number of oocytes and the top-quality embryo rate were significantly correlated with OPN embryo occurrence. Totally 112 OPN embryos were transferred in 70 cycles. The implantation rate of the cycles when OPN embryos were exclusively transferred was 17.0% with 2 miscarriages and 1 stillbirth observed. Of the 13 healthy infants born from 13 cycles, there were no reports of deformities. OPN derived blastocyst can obtain similar clinical pregnancy rate and implantation rate as those of 2PN blastocyst, but the rate of abortion was higher, with a significant difference. **Conclusion:** The appearance of OPN embryos in IVF can be considered as an indicator of a cycle with appropriate embryo development. Transferring OPN embryos should be taken into account when alternative embryos for transferring are not available.

Key words: abnormal fertilization; pronucleus (PN); pregnancy

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不孕女性的生育和心理压力对子宫内膜及内膜下血流的影响

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【摘要】目的: 探讨不孕女性的生育和心理压力与子宫内膜及内膜下血流的相关关系。方法: 采用生育压力(FPI)、心理压力(SRQ)、特质应对问卷(CSQ)、生活事件量表(LES)对115例初诊的不孕女性进行生育和心理压力测评。同时, 采用三维能量多普勒超声测量子宫内膜及内膜下容积、血管化指数(VI)、血流指数(FI)及血管化血流指数(VFI)。结果: FPI总分与子宫内膜及内膜下血流的FI显著相关($r_1=-0.248$, $r_2=-0.290$, $P<0.05$); 积极应对与子宫内膜及内膜下血流的FI具有相关性($r_3=0.210$, $r_4=0.242$, $P<0.05$); 生活事件与子宫内膜下VFI具有相关性($r_5=-0.191$, $P<0.05$); 且FPI的相关系数大于心理压力的相关系数。**结论:** FPI和积极应对与子宫内膜及内膜下血流的FI存在相关性, 要重点关注不孕女性的生育压力。

关键词: 不孕不育; 压力; 三维能量多普勒; 内膜下血流

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Impact of sterility and psychological stress on endometrial and subendometrial blood flow in female infertility

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【ABSTRACT】 Objective: To investigate the correlation between sterility and psychological stress and endometrial and subendometrial blood flow in female infertility. **Methods:** Totally 115 infertile women who came to the reproductive center at the first time were enrolled to the study. The fertility problem inventory (FPI), stress reaction questionnaire (SRQ), coping style questionnaire (CSQ), life event scale (LES) were adopted to evaluate sterility and psychological stress. Three-dimensional power Doppler sonography was performed to measure the endometrial and subendometrial volume (V), vascularization index (VI), blood flow volume index (FI) and vascular blood flow index (VFI). **Results:** FPI total score and endometrial and subendometrial FI was significantly correlated ($r_1=-0.248$, $r_2=-0.290$, $P<0.05$). The correlation coefficient of positive response and endometrial and subendometrial FI was statistically significant ($r_3=0.210$, $r_4=0.242$, $P<0.05$). The correlation coefficient of life events scores and endometrial VFI was also statistically significant ($r_5=-0.191$, $P<0.05$). The correlation coefficients of infertility pressure r_1 , r_2 were greater than those of r_3 , r_4 and r_5 . **Conclusion:** Infertility stress and positive coping were correlated with endometrial blood flow in a certain level. The infertility pressure should pay more attention during clinical practice.

Key words: infertility; pressure; three-dimensional power doppler ultrasound; subendometrial flow index

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· 综述 ·

生长激素对卵巢功能影响的研究进展

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【摘要】生长激素(growth hormone, GH)是由腺垂体前叶嗜酸性细胞分泌的一种肽类激素, 体内和体外实验显示 GH 可调节生殖过程, 它直接与卵巢上的生长激素受体(GH receptor, GHR)结合或通过胰岛素样生长因子(insulin-like growth factor, IGF)系统间接发挥作用, 从而刺激卵泡的生长、成熟, 易化排卵, 调节雌、孕激素的水平。近期研究证实 GH 可提高线粒体活性, 直接改善卵母细胞的质量。临床上, GH 常作为卵巢低反应(poor ovarian response, POR)或高龄患者的辅助治疗药物。

关键词: 生长激素(GH); 卵巢; 卵泡; 类固醇激素; 卵巢低反应(POR)

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• 综述 •

Research progress on the effect of growth hormone on ovarian function

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【ABSTRACT】 Growth hormone is a kind of peptide hormone, which is secreted by eosinophils in ademohypophysis. *In vivo* and *in vitro* experiments indicate that growth hormone (GH) has a role in reproductive processes. It regulates follicular growth, maturation, ovulation and the level of estradiol and progesterone by directly combining with the growth hormone receptors (GHR) in the ovary or connecting with the insulin-like growth factor (IGF) system indirectly. Recent studies have confirmed that GH promotes the activity of mitochondria and improves the oocytes quality. In clinical practice, GH is typically used as an adjuvant therapy for poor ovarian response (POR) or elderly patients. This article summarizes the physiological function of GH and its mechanism on the ovary, as well as expounds the effects of GH on ovarian function from the aspects of follicular growth, maturation, ovulation and the regulation of steroids.

Key words: growth hormone (GH); ovary; follicle; steroid hormone; poor ovarian response (POR)

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抗苗勒管激素在预测卵泡发育与 卵母细胞质量的研究进展

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【摘要】 抗苗勒管激素(anti-Müllerian hormone, AMH)由自分泌、旁分泌产生,主要通过II型跨膜丝氨酸/苏氨酸激酶受体发挥作用,可以抑制原始卵泡募集,阻碍卵泡生长发育,并参与调节颗粒细胞类固醇生成。卵泡液AMH不仅在小窦卵泡中表达,在排卵前大窦卵泡中仍持续表达,通过直接调节各种细胞因子的表达,参与调控卵母细胞成熟的最后阶段,即AMH表达量逐渐减少是卵泡优势化的必备条件,从而影响卵母细胞的质量,在预测卵巢储备方面发挥重要作用,也是预测卵泡发育和卵母细胞质量的重要指标。而血清AMH与卵母细胞质量之间的关系仍存在争议。

关键词: 抗苗勒管激素(AMH); 卵母细胞质量; 妊娠率; 胚胎质量; 辅助生殖

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Research progress of anti-Müllerian hormone in predicting follicular development and oocyte quality

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【ABSTRACT】 Anti-Müllerian hormone (AMH) is a dimeric glycoprotein, which belongs to the transforming growth factor beta (TGF- β) family, it plays an important role in the prediction of ovarian reserve, and also is an important index of follicular development and oocyte quality. Studies show that AMH plays its role through transmembrane serine/threonine kinase receptor II, which can inhibit the recruitment of primordial follicles, stunt the growth and development of follicles, and it also participates in the regulation of steroid production in granulosa cells. Follicular fluid AMH is a good indicator for predicting oocyte quality because it can directly affect oocytes through a variety of cytokines, but the relationship between serum AMH and oocyte quality remains controversial. Therefore, AMH has a broad prospects in research and application of assisted reproduction.

Key words: anti-Müllerian hormone (AMH); oocyte quality; pregnancy rate; embryo quality; assisted reproduction

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人卵母细胞辅助激活研究进展

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【摘要】 卵胞质内精子注射(intracytoplasmic sperm injection, ICSI)是目前治疗男性不育最有效的方法,但在ICSI周期中仍然有1%~3%的受精失败发生。近年来逐渐发展起来的卵母细胞辅助激活(assisted oocyte activation, AOA)技术在改善ICSI后受精失败患者的妊娠结局方面取得了较为明显的效果,有望成为治疗男性不育的重要辅助手段。本文综述了卵母细胞激活机制领域的研究成果,揭示了精子中的PLC ξ 蛋白引起卵母细胞内Ca²⁺震荡进而触发激活的机制,介绍了目前对ICSI受精失败患者精子激活能力的检测与诊断方法,以及不同卵母细胞辅助激活技术如电激活, Ca²⁺载体和SrCl₂等激活技术的研究现状,并总结了这些技术在安全性方面所获得的证据,在此基础上对AOA技术今后的发展方向和前景作了探讨。

关键词: 辅助激活 (AOA); Ca²⁺震荡; 受精失败; 人卵母细胞

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Current achievements of assisted oocyte activation in human

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【ABSTRACT】 Even though intracytoplasmic sperm injection (ICSI) is thought to be the most effective treatment for male infertility, 1%–3% fertilization failure still occurred following ICSI. Assisted oocyte activation (AOA) has been developed for improving pregnancy outcome of patients suffering fertilization failure following ICSI, and been possible to become an important assisted technology in male infertility treatment. We reviewed the achievements in oocyte activation mechanism of human, and described the mechanism that PLC ξ in sperm activated oocyte by causing intracellular Ca²⁺ oscillations, and introduced the diagnostic tools for sperm activating capability of patients, and the current research status of different AOA technologies, such as electrical activation, Ca²⁺ ionophore, and SrCl₂ activation, and furthermore we summarized evidences in safety of AOA technologies, and then discussed prospect and development of AOA technology in future.

Key words: assisted oocyte activation (AOA); Ca²⁺ oscillating; fertilization failure; human oocyte

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外泌体在子痫前期发病机理中的研究进展

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【摘要】外泌体(exosome)是由多种细胞分泌的膜性纳米囊泡,携带蛋白、mRNA、miRNA和脂质等内含物,通过靶细胞传递内含物,介导细胞与细胞之间的通讯。孕妇血浆中由胎盘释放的外泌体浓度是未孕女性的50倍,子痫前期患者体内外泌体的蛋白和miRNA的表达水平发生了变化,使母体滋养细胞侵袭能力不足、降低内皮细胞的功能和血管生成能力,导致子痫前期等病理性妊娠。所以孕妇血浆中外泌体表达谱的改变可应用于胎盘功能紊乱的临床诊断。

关键词: 外泌体(exosome); 子痫前期; miRNA

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Research advances of exosome in the pathogenesis of preeclampsia

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【ABSTRACT】 Exosomes are nanometric membrane vesicles secreted by various cell types, which are enriched in inclusions, such as proteins, mRNA, miRNA, lipids, and so on. Exosomes mediate cell-cell communication via transferring the inclusions to the target cells. The placenta-derived exosome concentration in the plasma of pregnant group is 50 times more than that of non-pregnant group. The expression levels of exosomal proteins and miRNA in preeclampsia patients have changed, resulting in the limited invasion ability of maternal trophoblast cells, decline of endothelial cell function and angiogenesis ability, and further causing pathological pregnancy of preeclampsia. Therefore, the expression changes of plasma exosomes can be used for clinical diagnosis of placental function disorder.

Key words: exosome; preeclampsia; miRNA

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雌激素与女性认知功能关系的研究进展

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【摘要】随着女性平均预期寿命的延长及阿尔茨海默病(alzheimer disease, AD)的发病率明显上升, 雌激素与女性认知功能的关系研究成为当今学术界研究的热点之一。细胞培养和动物实验数据已经证实, 雌激素能通过多种途径保护认知功能相关区域的神经细胞, 进而提高认知功能。但是学者们对雌激素水平和女性认知功能的相关性问题, 及激素补充治疗(HRT)对围绝经期及绝经后女性认知功能是否有保护作用仍有争议。多数研究表明雌激素水平和女性认知功能是相关的, 但是不同的人群, 不同时期, 不同的认知测试可能会有不同结果。激素补充治疗能否提高女性认知功能取决于研究人群、治疗时机、药物种类及个体化用药等。

关键词: 认知功能; 雌激素; 记忆; 激素补充治疗(HRT); 绝经

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Research progress of relationship between estrogen and cognition in women

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【ABSTRACT】 As the increasing of women's life expectancy and the rising of the incidence rate of Alzheimer disease (AD), the study on the relationship between estrogen and cognition in women becomes one of the pop topics in today's academia. Several cell culture and animal studies have suggested that estrogen can have protective effects on the neurons in cognition-related brain areas to influence cognitive function, but studies of the association between levels of estrogen and cognitive function in women, as well as the effects of hormone replacement therapy (HRT) given to perimenopausal and postmenopausal women, have produced inconsistent and complex results. However, most of the studies have recently found that levels of estrogen are associated with cognitive function in women, but the results may vary in different subjects, periods and using different cognitive tests. HRT can improve cognitive function in women or not may depend on the study population, treatment opportunity, the type of drugs, individualized medication and so on.

Key words: cognition; estrogen; memory; hormone replacement therapy (HRT); menopause

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• 临床报道 •

体外受精中3原核胚胎的发育 及可利用价值的探讨

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【摘要】目的: 探讨体外受精(IVF)中异常的3原核(PN)胚胎的发育及可利用价值。方法: 收集IVF治疗周期中废弃的3PN受精卵204个进行体外培养, 观察其发育能力, 并与同周期的1138个2PN受精卵进行比较; 采用胚胎植入前遗传学筛查(PGS)技术对由3PN发育成的19枚囊胚进行非整倍体分析。结果: 3PN组和2PN组的卵裂率无统计学差异($P>0.05$); 但3PN组囊胚形成率显著低于2PN组[9.6%(19/97) vs 37.9%(204/342), $P<0.01$]。整倍体分析显示, 10.5%(2/19)的3PN来源的囊胚为正常二倍体核型。结论: 3PN受精卵有继续发育能力; 囊胚培养和高通量测序可作为有效筛选异常PN受精卵中正常核型胚胎的一种方法。

关键词: 3原核(PN)胚胎; 囊胚; 体外培养; 高通量测序(HTS); 整倍体分析

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• 临床报道 •

**Exploration of the development and utility of tripronuclear embryos
after *in-vitro* fertilization**

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【ABSTRACT】 Objective: To explore the development and utility value of tripronuclear (3PN) embryos after conventional *in-vitro* fertilization (IVF). **Methods:** Totally 204 discarded 3PN zygotes were cultured during IVF and developmental potentiality of 3PN zygotes was compared with bipronuclear (2PN) zygotes. Preimplantation genetic screening (PGS) technology was employed to investigate aneuploid of 19 3PN blastocysts. **Results:** 3PN and 2PN groups demonstrated equal cleavage rates, but 3PN group showed lower blastocyst formation rate, and some 3PN blastocysts had normal diploid karyotype. **Conclusion:** Blastocyst culture and high-throughput sequencing (HTS) were effective methods for screening normal karyotype embryos from abnormal pronucleus zygotes.

Key words: tripronuclear (3PN) embryos; blastocyst; *in vitro* culture; high-throughput sequencing (HTS); euploid analysis

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· 个案报道 ·

辅助生殖技术助孕后不同步异位妊娠 原因探究及文献回顾

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【摘要】目的: 探讨辅助生殖技术(ART)能够降低异位妊娠风险的预防、治疗措施。方法: 报道2例国内外少见的不同步异位妊娠病例, 并结合近年来相关的5个案例进行回顾性分析。结果: 不同步异位妊娠成因复杂, 自然受孕及ART助孕都可发生, 最迟可发生在初次异位妊娠后1个月左右, 且往往需要2次手术治疗。结论: 对有相应适应证的患者, 输卵管抽芯切除作为预处理或冻融单囊胚移植可降低不同步异位妊娠的发生率; 异位妊娠手术处理后1个月左右均需密切监测患者情况, 尽早发现不同步异位妊娠病灶并给予及时处理。

关键词: 辅助生殖技术(ART); 不同步异位妊娠; 多部位异位妊娠

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• 个案报道 •

Investigation and literature review about heterochronic ectopic pregnancy after ART

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【ABSTRACT】 Objective: To discuss the prevention and treatment measures that can reduce the risk of ectopic pregnancy of assisted reproductive technology (ART). **Methods:** Two unusual cases of heterochronic ectopic pregnancy have been reported. A retrospective clinical study was performed to analyze the five relevant cases in recent years. **Results:** The cause of heterochronic ectopic pregnancy was complicated. This kind of ectopic pregnancy could be spontaneously or related to ART. It could be happened about one month after the first ectopic pregnancy at the latest, and the patient was often required the second surgical treatment. **Conclusion:** The patient with tubal factor can be treated with laparoscopic “core-pulling” salpingectomy before IVF. Vitrified-thawed single-blastocyst was another great solution to reduce the potential heterochronic ectopic pregnancy rates. The patient should be monitored continuously after the operation of ectopic pregnancy a month or so, heterochronic ectopic pregnancy should be discovered and treated timely.

Key words: assisted reproductive technology (ART); heterochronic ectopic pregnancy; multiple site ectopic pregnancy

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