·临床研究.

超短方案在高龄体外受精患者中的应用

童婧 郑中 孙赟 洪燕 高敏芝 赵晓明

200135上海交通大学医学院附属仁济医院生殖医学中心,上海市辅助生殖与优生重点实验室通信作者: 赵晓明, Tel: +86-21-20284564, Email: zhao xiao ming@126.com

DOI: 10.3760/cma.j.issn.2096-2916.2017.11.001

【摘要】目的 探讨超短方案在高龄患者进行体外受精-胚胎移植(*in vitro* fertilization-embryo transfer, IVF-ET)中的疗效。方法 回顾性分析 326 例年龄>38 岁女性的 IVF-ET 周期的临床资料,根据不同促排卵方案分为超短方案组和微刺激方案组。比较和分析 2 种促排卵方案的疗效。结果 超短方案组的获卵数(5.8 \pm 0.3)、正常受精数(3.5 \pm 0.2)、优质胚胎数(2.5 \pm 1.8)和有效胚胎数(2.6 \pm 0.2)均高于微刺激方案组(2.4 \pm 0.1, 1.5 \pm 0.1, 1.0 \pm 1.0, 1.7 \pm 0.1)(P<0.001);患者的卵裂率和优质胚胎率组间无统计学差异(P>0.05)。但超短方案组每取卵周期累积妊娠率(40.00%)和累积活产率(8.41%)均高于微刺激方案组(30.00%,7.52%)(P<0.001),新鲜胚胎移植取消率(47.00%)明显低于微刺激方案组(99.56%)(P<0.001)。结论 对于高龄IVF患者进行促排卵时使用超短方案,可以获得更多的卵母细胞和有效胚胎,增加每取卵周期的累积妊娠率和活产率,并且通过降低新鲜胚胎移植取消率,减少患者的心理负担,对于高龄IVF患者是一种比较好的选择。

【关键词】 体外受精 - 胚胎移植(IVF-ET); 高龄; 超短方案; 微刺激方案; 累积妊娠率; 累积活产率基金项目: 国家自然科学基金项目(81370687)

Effect of ultrashort protocol in advanced aged patients undergoing in vitro fertilization-embryo transfer procedures

Tong Jing, Zheng Zhong, Sun Yun, Hong Yan, Gao Minzhi, Zhao Xiaoming

Center for Reproductive Medicine, Renji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai Key Laboratory for Assisted Reproduction and Reproductive Genetics, Shanghai 200135, China (Tong J, Zheng Z, Sun Y, Hong Y, Gao MZ, Zhao XM)

Corresponding author: Zhao Xiaoming, Tel: +86-21-20284564, Email: zhao xiao ming@126.com

[Abstract] Objective To investigate the effect of ultrashort protocols in advanced age patients undergoing *in vitro* fertilization-embryo transfer (IVF-ET) procedures. **Methods** The IVF-ET cycles of 326 women (>38 years old) were retrospectively analyzed. The patients were divided into ultrashort group and mild group according to the ovarian stimulation protocols. Then the effect of the two ovarian stimulation protocols was compared and analyzed. **Results** The numbers of oocytes retrieved (5.8 ± 0.3) , normally fertilized zygotes (3.5 ± 0.2) , top-quality embryos (2.5 ± 1.8) and embryos suitable for transplantation (2.6 ± 0.2) were significantly higher in the ultrashort group than those in the mild group $(2.4\pm0.1, 1.5\pm0.1, 1.0\pm1.0, 1.7\pm0.1)$ (P<0.001). The cleavage rate and the top-quality embryo rate showed no significant difference between the two groups (P>0.05). But the cumulative pregnancy rate (40.00%) and the cumulative live birth rate per retrieval cycle (8.41%) in the ultrashort group were significantly higher than those in the mild group (30.00%, 7.52%) (P<0.001). The cancellation rate of fresh embryo transfer in ultrashort group (47.00%) was significantly lower than that in the mild group (99.56%) (P<0.001). **Conclusion** The ultrashort protocol is a better choice for the advanced age patients who underwent IVF-ET procedures, because it can bring more oocytes and embryos suitable for transplantation and increase the cumulative pregnancy rate and live birth rate per retrieval cycle consequently. Also it can reduce the cancellation rate of fresh embryo transfer and the psychological burden of patients at the same time.

[Key words] In vitro fertilization-embryo transfer (IVF-ET); Advanced age; Ultrashort protocol; Mild protocol; Cumulative pregnancy rate; Cumulative live birth rate

Fund program: National Natural Science Foundation of China (81370687)

辅助生殖技术中阴道局部给药黄体支持方案中血清低孕酮水平的临床疗效研究

周媛萍 吴晓云 朱玉蓉 徐键

310006 杭州, 浙江大学医学院附属妇产科医院生殖医学中心(周媛萍、徐键); 313000 浙江省湖州市妇幼保健院生殖医学中心(周媛萍、吴晓云、朱玉蓉)

通信作者: 徐键, Tel: +86-13588888666, Email: xuj@zju.edu.cn

DOI: 10.3760/cma.j.issn.2096-2916.2017.11.002

【摘要】目的 探讨辅助生殖技术(ART)中阴道局部给药的黄体支持方案血清低孕酮(P)水平对临床疗效的影响。方法 选取 2012 年 6 月—2016 年 12 月期间行激素替代方案冻融胚胎移植(FET)的 624 个周期,按照移植后黄体支持方案的不同分为 A 组(黄体酮阴道缓释凝胶+地屈孕酮组,348 个周期)和 B 组(黄体酮针剂+地屈孕酮组,276 个周期),比较组间、组内移植 14 d 妊娠与非妊娠者的血清 P 水平及妊娠结局。结果 ①移植 14 d A 组中妊娠者与非妊娠者血清 P 水平无统计学差异(P>0.05),B 组中妊娠者血清 P 水平[(74.08 ± 24.80) nmol/L]明显高于非妊娠者[(62.28 ± 29.34) nmol/L],差异有统计学意义(P<0.05)。② A 组妊娠者的 P 水平[(16.07 ± 9.40) nmol/L]明显低于 B 组,差异有统计学意义(P<0.05)。③胚胎着床率、临床妊娠率、早期流产率、异位妊娠率组间无统计学差异(P>0.05)。结论 黄体酮阴道缓释凝胶作为黄体支持应用于胚胎移植术后,与肌肉注射黄体酮具有相似的临床疗效,但由于其具有子宫首过效应,血清中表达水平低,无需进行血清 P 水平的监测。

【关键词】 辅助生殖技术(ART); 黄体支持; 黄体酮阴道缓释凝胶

A clinical study on the level of serum low progesterone about luteal phase support for partial vaginal delivery in assisted reproductive technology Zhou Yuanping, Wu Xiaoyun, Zhu Yurong, Xu Jian Obstetrics and Gynecology Hospital Affiliated to Zhejiang University for Reproductive Medicine Center, Hangzhou 310006, China (Zhou YP, Xu J); Huzhou Women and Children Hospital for Reproductive Medicine Center, Huzhou 313000, China (Zhou YP, Wu XY, Zhu YR)

Corresponding author: Xu Jian, Tel:+86-13588888666, Email: xuj@zju.edu.cn

[Abstract] Objective To investigate the effects of low progesterone levels on the clinical efficacy of the luteal support protocol by using vaginal progesterone gel in assisted reproductive technology (ART). Methods A total of 624 cycles of frozen-thawed embryo transfer (FET) with hormone replacement were performed in our center from June 2012 to December 2016. They were divided into two groups according to the difference in the post luteal support protocol: group A (progesterone vaginal sustained release gel + dydrogesterone) 348 cycles and group B (progesterone injection + dydrogesterone) 276 cycles. The serum progesterone levels and pregnancy outcome were compared in the two groups of pregnant and non-pregnant women with 14 d after embryo transfer. Results 1) There were no significant differences in serum progesterone levels between the pregnant and non-pregnant groups in group A after 14 d of transplantation (P>0.05). The level of serum progesterone in group B [(74.08 ± 24.80) nmol/L] was significantly higher than that of non-pregnant women [(62.28 ± 29.34) nmol/L] after 14 d of transplantation, and the difference was statistically significant (P<0.05). 2) The progesterone level in group A $[(16.07 \pm 9.40) \text{ nmol/L}]$ was significantly lower than that in group B, the difference was statistically significant (P<0.05). 3) The rate of embryo implantation, the rate of clinical pregnancy, the rate of early abortion and the rate of ectopic pregnancy were not statistically different between the two groups (P>0.05). Conclusion Progesterone vaginal sustained-release gel as a luteal support in the treatment of embryo transfer, has the same efficacy with intramuscular progesterone injection. But because it has the first-pass effect of uterus, the expression level in serum is low, so the monitoring of serum progesterone level is not needed.

[Key words] Assisted reproductive technology (ART); Luteal support; Progesterone vaginal sustained-release gel

孕激素对促排卵过程中抑制素水平的影响

叶静 陈秋菊 何雯 张洁 叶红娟 傅永伦 吕祁峰 匡延平

200011 上海交通大学医学院附属第九人民医院辅助生殖科

通信作者: 匡延平, Tel: +86-21-23271699*5539, Fax: +86-21-53078108,

Email: Kuangyanp@126.com

DOI: 10.3760/cma.j.issn.2096-2916.2017.11.003

【摘要】目的 探讨卵巢储备功能正常的妇女在促排卵过程中孕激素对抑制素水平的影响,分析高孕激素状态下促排卵(PPOS)的内分泌特征及随后的冻融胚胎移植(FET)结局。方法 93 例接受体外受精/卵胞质内单精子注射(IVF/ICSI)治疗的卵巢储备功能正常者随机分到研究组(PPOS 组, n=60)和对照组(短方案组, n=33),测定促排卵过程中(月经周期第 3 日、第 10~12 日、诱发排卵日、诱发排卵次日)激素水平、抑制素 A 和抑制素 B 表达水平。所有患者采取全部胚胎冷冻的策略,分析后续 FET 周期的结果。结果 在研究组,抑制素 A 和 B 的水平随着促排卵过程的继续均呈现增长的趋势,诱发目的抑制素水平[抑制素 A 为(1 416.4 ± 924.7) pg/mL,抑制素 B 为(1 188.5 ± 819.1) pg/mL]较基础水平[抑制素 A 为(29.7 ± 23.4) pg/mL,抑制素 B 为(82.5 ± 49.4) pg/mL]均有明显增加(P<0.05),诱发排卵次日的抑制素 A 水平较诱发日明显增加,达到(2 046.7 ± 1 280.5) pg/mL(P<0.05),而诱发排卵次日的抑制素 B 水平较诱发日略有下降(P>0.05)。获卵数组间无统计学差异,在随后的 FET 周期中,两组的临床妊娠率、种植率、活产率均无统计学差异(P>0.05)。结论 促排卵过程中的高孕激素水平没有影响卵泡周围颗粒细胞分泌抑制素。安宫黄体酮(MPA)联合人绝经期促性腺激素(hMG)进行 PPOS 可以获得具有发育潜力的胚胎,在随后的 FET 周期中,可以获得满意的妊娠结局。

【关键词】 孕激素; 抑制素; 高孕激素状态下促排卵(PPOS)

基金项目: 国家自然科学基金(31071275, 81270749, 31101070); 上海市自然科学基金(11411950105)

.临床研究.

Impact of progesterone on inhibins during controlled ovarian stimulation Ye Jing, Chen Qiuju, He Wen,

Zhang Jie, Ye Hongjuan, Fu Yonglun, Lyu Qifeng, Kuang Yanping

Department of Assisted Reproduction, Shanghai Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai 200011, China (Ye J, Chen QJ, He W, Zhang J, Ye HJ, Fu YL, Lyu QF, Kuang YP)

Corresponding author: Kuang Yanping, Tel: +86-21-23271699*5539, Fax: +86-21-53078108,

Email: Kuangyanp@126.com

[Abstract] Objective To explore the impact of progesterone on inhibins during progestin-primed ovarian stimulation (PPOS) in women with normal ovarian reserve and to compare cycle characteristics and pregnancy outcomes in subsequently frozen-thawed embryo transfer (FET) cycles. Methods Totally 93 patients undergoing in vitro fertilization/intracytoplasmic sperm injection-embryo transfer (IVF/ICSI-ET) were randomized to study group (PPOS, n=60) or control group (short protocol, n=33). Serum hormones were detected on day 3, day 10–12, the trigger day and the day after trigger (approximate 10 h after trigger). Viable embryos were cryopreserved for later transfer in both protocols. Outcomes of FET were analyzed further. Results
In study group, inhibins value significantly increased during ovarian stimulation, and average inhibins level [inhibin A (1416.4 ± 924.7) pg/mL, inhibin B (1188.5 ± 819.1) pg/mL] on the trigger day was significantly higher than the basal levels [inhibin A (29.7 \pm 23.4) pg/mL, inhibin B (82.5 \pm 49.4) pg/mL](P<0.05). Inhibin A value increased significantly to (2 046.7 \pm 1 280.5) pg/mL at the day after trigger. Serum inhibin B slightly decreased on the day after trigger later compared with the trigger day, but didn't reach any statistical significance. The number of oocytes retrieved in study group was similar to those in the controls. No statistically significant differences were found in the clinical pregnancy rate, implantation rate, and livebirth rate in study group and control group. Conclusion High-level progesterone didn't affect the granulosa cells secretion function of inhibins during controlled ovarian stimulation. Medroxyprogesterone acetate (MPA) combined with human menopause gonadotropin (hMG) can obtain competent oocytes/embryos in women undergoing IVF/ICSI treatments, with optimal pregnancy outcomes in FET cycles.

(Key words) Progesterone; Inhibins; Progestin-primed ovarian stimulation (PPOS)

Fund program: National Nature Science Foundation of China (31071275, 81270749, 31101070); Natural Science Foundation of Shanghai (11411950105)

辅助生殖技术对人胎盘 DNA 甲基化水平的影响

郭翔宇 贾青钨 陈书强 董杰 王鑫 王晓红 710032 西安, 第四军医大学唐都医院生殖医学中心

通信作者: 王晓红, Tel: +86-13991262559, Email: wangxh-99919@163.com

DOI: 10.3760/cma.j.issn.2096-2916.2017.11.004

【摘要】目的 探究辅助生殖技术(ART)助孕对单胎足月分娩新生儿的胎盘及胎盘总 DNA 甲基化水平和甲基化相关基因表达的影响。方法 选择 2016 年 6 月—2016 年 12 月期间单胎足月分娩的患者,ART 子代为 ART 组,自然妊娠子代为对照组,两组按孕妇年龄、孕周等进行配对后,比较两组胎盘质量、新生儿体质量、胎盘效率。采用酶联免疫吸附测定法(ELISA)测定胎盘总 DNA 的甲基化水平,采用实时定量聚合酶链式反应(RT-qPCR)方法检测胎盘甲基转移酶(DNA methyltransferase, DNMT)家族和去甲基化酶(ten-eleven translocation, TET)家族的 mRNA 表达水平。结果 ① ART 组新生儿体质量[(3 650.50 ± 393.84) g]、胎盘重量[(633.05 ± 98.58) g]显著增加,且高于对照组[(3 339.50 ± 377.01) g, (563.00 ± 85.60) g] (P<0.05)。② ART 组胎盘总 DNA 甲基化水平(1.22% ± 0.45%)显著低于对照组(2.08% ± 0.98%)(P<0.05)。③ ART 组 DNMT3B、TET1、TET2、TET3 的 mRNA 相对表达量分别为 4.61 ± 1.06、4.66 ± 1.06、4.99 ± 1.09、4.92 ± 1.13,显著高于对照组(1.23 ± 0.55、1.27 ± 0.56、1.47 ± 0.50、1.41 ± 0.61) (P<0.05),DNMT1、DNMT3A 的表达水平无统计学差异(P>0.05)。结论 ART 会导致人类妊娠晚期胎盘过度生长,总 DNA 甲基化水平降低,DNMT3B、TET1、TET2、TET3 表达上调可能是导致胎盘 DNA 甲基化水平降低的机制。

【关键词】 辅助生殖技术(ART); 胎盘; 甲基化; 甲基转移酶(DNMT); 去甲基化酶(TET) 基金项目: 国家自然科学基金-面上项目究(81671463); 陕西省重点研发计划重点项目(2017ZDCXL-SF-02-03)

Effects of assisted reproductive technology on the level of DNA methylation in human placenta

Guo Xiangyu, Jia Qingge, Chen Shuqiang, Dong Jie, Wang Xin, Wang Xiaohong Reproductive Medicine Center, Tangdu Hospital, the Forth Military Medical University, Xi'an 710032, China (Guo XY, Jia QG, Chen SQ, Dong J, Wang X, Wang XH)

Corresponding author: Wang Xiaohong, Tel: +86-13991262559, Email: wangxh-99919@163.com

[Abstract] Objective To explore whether assisted reproductive technology (ART) affects the infant body weight, the placental weight, ratio of infant/placental weight, the mean DNA methylation level and the expression level of DNA methyltransferase (DNMT) family and ten-eleven translocation (TET) family. Methods The infant weight, placental weight, ratio of infant/placental weight were compared between 35 singleton full-term neonates derived from ART-born (ART group) and 36 singleton full-term neonates derived from naturally-born (negative control group, NC group). To avoid the effects of age factors, 20 placentas were selected from each group to detect the mean DNA methylation level by ELISA and the expressions of DNMT family (DNMT1, DNMT3A, DNMT3B) and TET family (TET1, TET2, TET3) by RT-qPCR. **Results** The infant weight $[(3.650.50\pm393.84)]$ g and placental weight [(633.05 \pm 98.58) g] were significantly increased in ART group compared with NC group [(3 339.50 \pm 377.01) g, (563.00 ± 85.60) g]. The mean DNA methylation level of placenta in ART group $(1.22\%\pm0.45\%)$ was significantly lower than that in NC group (2.08% \pm 0.98%). The mRNA expression levels of DNMT3B, TET1, TET2, TET3 were up-regulated in ART group (4.61 \pm 1.06, 4.66 \pm 1.06, 4.99 \pm 1.09, 4.92 \pm 1.13) compared with control group (1.23 \pm 0.55, 1.27 ± 0.56 , 1.47 ± 0.50 , 1.41 ± 0.61) (P < 0.05), though there were no significant differences in the mRNA expression lever of *DNM*T1 and *DNM*T3A. **Conclusion** ART can lead to the overgrowth of placenta in the late stage of human pregnancy and a low level of DNA methylation in the placenta, which may due to the up-regulated expression level of DNMT3B, TET1, TET2, TET3.

[Key words] Assisted reproductive technology (ART); Placenta; Methylation; DNA methyltransferase (DNMT); Ten-eleven translocation (TET)

Fund program: Surface of National Natural Science Foundation of China (81671463); Key Project of Shaanxi Provincial Key Research and Development Plan (2017ZDCXL-SF-02-03)

钙网蛋白介导的凋亡在早期先兆流产过程中 的作用

邓小月 柳长柏 熊焱强 秦琪 李志英

443001 宜昌, 三峡大学第二临床医学院(邓小月、熊焱强、秦琪、李志英); 443002 宜昌, 肿瘤 微环境与免疫治疗湖北省重点实验室(柳长柏)

通信作者: 李志英, Tel: +86-717-6556403, Fax: +86-717-6555530, Email: zhiying969@126.cn

DOI: 10.3760/cma.j.issn.2096-2916.2017.11.005

【摘要】目的 探讨不同表达水平的钙网蛋白(calreticulin, CRT)与先兆流产的关系。方法 ①分别应用免疫组织化学法、Western blotting 和 qPCR 检测早期正常妊娠(n=35, 均因非意愿妊娠而要求人工流产)及早期先兆流产患者人工流产后的蜕膜和绒毛组织中 CRT 蛋白及 mRNA 的表达。②分别转染合成并经检测的质粒 mEmerald-CRT 与 CRT-siRNA 至 BeWo 细胞中,检测 CRT 及 Caspase-3 的表达。结果 免疫组织化学可见CRT阳性信号定位于绒毛两层滋养层细胞的胞质和胞膜上,先兆流产组染色比正常早孕组深、面积大; qPCR 与Western blotting检测CRT表达量在先兆流产组明显高于正常早孕组,先兆流产组中mRNA表达量为正常早孕组的 1.2 倍(P<0.05)。 qPCR 与 Western blotting 检测 CRT 与 Caspase-3 表达量在质粒 (mEmerald-CRT)转染组高于对照组,质粒转染组中 CRT 及 Caspase-3 的表达量分别是对照组的 3.5 倍与 2 倍 (P<0.05),在 si-RNA 组低于对照组,对照组中 CRT 及 Caspase-3 的表达量分别 si-RNA 组的 5 倍与 2 倍 结论 早期先兆流产的发生可能与 CRT 在绒毛和蜕膜组织中的高表达并介导凋亡相关。

【关键词】 钙网蛋白; 绒毛; 蜕膜; 早期先兆流产; 细胞凋亡

Effects of calreticulin mediated apoptosis during the early threatened abortion Deng Xiaoyue,

Liu Changbai, Xiong Yanqiang, Qin Qi, Li Zhiying

The Second Medical School, China Three Gorges University, Yichang 443001, China (Deng XY, Xiong YQ, Qin Q, Li ZY); Three Gorges University Hubei Key Laboratory of Tumor Microenvironment and Immunotherapy, Yichang 443002, China (Liu CB)

Corresponding author: Li Zhiying, Tel: +86-717-6556403, Fax: +86-717-6555530, Email: zhiying969@126.cn

[Abstract] Objective To explore the relationship between the expression level of calreticulin (CRT) and early threatened abortion by observing CRT expression level in decidua and villi tissues. Methods 1) The decidua and villi tissues of normal pregnancies and early threatened abortion patients were collected and treated respectively. 2) The expression of CRT protein was verified by immunohistochemistry and Western blotting, and the expression of CRT mRNA was detected by qPCR. 3) The plasmid mEmerald-CRT was synthesized and detected. 4) CRT-siRNA was synthesized and detected. 5) Plasmid mEmerald-CRT and CRT-siRNA were transfected into BeWo cells respectively and the expressions of CRT and Caspase-3 were detected by Western blotting and qPCR. Results 1) The decidua and villi tissues of normal pregnancies (35 cases) and early threatened abortion (40 cases) were collected. 2) Immunohistochemistry showed that the stains were deeper and bigger in early threatened abortion group than the normal pregnancy group; qPCR test and Western blotting showed the expression of CRT was significantly higher in early threatened abortion than that in normal pregnancy, the expression of mRNA in early threatened abortion groups was 1.2 times of normal pregnancy (P<0.05). 3) qPCR test and Western blotting showed CRT and Caspase-3 in mEmerald-CRT groups were significantly higher than those in control groups, the expressions of CRT and Caspase-3 in mEmerald-CRT groups were 3.5 times and 2 times of control groups respectively (P<0.05). 4) qPCR test and Western blotting showed CRT and Caspase-3 in CRT-siRNA groups were significantly lower than those in control groups, the expressions of CRT and Caspase-3 in CRT-siRNA groups were 5 times and 2 times of control groups, respectively (P<0.05). **Conclusion** The occurrence of early threatened abortion may be related to excessive CRT expression and its mediated abnormal apoptosis in decidua and villi tissues.

[Key words] Calreticulin; Decidua; Villi; Early threatened abortion; Cell apoptosis

短时受精中不同受精结局组间精子-透明质酸结合率及妊娠率的比较

杨雪莲 赵焕 罗宇富

518001 深圳市武警医院生殖中心

通信作者: 杨雪莲, Tel: +86-755-82267770, Email: cqy_jz@126.com

DOI: 10.3760/cma.j.issn.2096-2916.2017.11.006

【摘要】目的 探讨精子 - 透明质酸结合率对受精能力的预测以及妊娠的影响。方法 回顾性分析 2016年1月—6月期间本中心正常受精的短时体外受精(IVF)患者 1 630 例作为对照组(短时 IVF 组), 因短时 受精失败行补救卵胞质内单精子注射(ICSI)的 130 例作为研究组(R-ICSI 组), 检测并分析两组精液的精子 - 透明质酸结合率、浓度、前向运动率、正常形态率、胚胎质量以及妊娠结局。结果 ①女方年龄、不孕年限、总 Gn 用量、Gn 使用时间以及获卵数组间均无统计学差异(P>0.05); ② R-ICSI 组的精子 - 透明质酸结合率[(63.8 ± 17.4)%]显著低于短时 IVF 组[(71.8 ± 13.6)%](P<0.01), 并同时伴有精子浓度和正常形态率的明显下降(P<0.05), 但其均值却仍然高于精液常规参数的正常参考值; ③R-ICSI 组的正常受精率(70.8%)、总受精率(76.2%)及优质胚胎率(50.0%)均显著低于短时 IVF 组(76.01%, 85.0%, 59.0%)(P<0.01); ④ R-ICSI 组平均移植胚胎数(2.0 ± 0.2)显著高于短时 IVF 组(1.9 ± 0.3)(P<0.01), 但种植率(36.6%)却仍然低于短时 IVF 组(49.0%)(P<0.05); R-ICSI 组临床妊娠率低于短时 IVF 组, 胚胎停育率高于短时 IVF 组, 但两者之间的差异并无统计学意义(P>0.05)。结论 精子 - 透明质酸结合率对 IVF 有一定的预测作用, 结合常规参数, 精子 - 透明质酸结合率低于 63.8%时,受精失败风险增加,但其对于妊娠的影响还有待于进一步研究。

【关键词】 受精失败; 精子-透明质酸结合率; 妊娠结局

Comparison of sperm-hyaluronan binding rate and pregnancy rate between different fertilization outcome groups in short-term in vitro fertilization Yang Xuelian, Zhao Huan, Luo Yufu Reproductive Center of Shenzhen Military Hospital, Shenzhen 518001, China (Yang XL, Zhao H, Luo YF) Corresponding author: Yang Xuelian, Tel: +86-755-82267770, Email: cqy jz@126.com

[Abstract] Objective To detect the prediction of sperm-hyaluronan binding rate for fertilization and influence of pregnancy. Methods A retrospective analysis from January to June in 2016 was performed on patients who took short-term fertilization for the first time in our center. All the patients were divided into two groups, one was control group which took conventional in vitro fertilization (IVF) including 1 630 patients, the other was experimental group including 130 patients which took rescue intracytoplasmic sperm injection (R-ICSI). The rate of sperm-hyaluronan binding, concentration, forward movement rate, normal morphology rate, embryo quality and pregnancy outcome were compared. Results 1) There were no differences in female age, infertility duration, total dosage of Gn used, duration of Gn used and number of oocytes retrieved between the two groups (P>0.05). 2) The rate of sperm-hyaluronan binding in R-ICSI group [(63.8 ± 17.4)%] was significantly lower than that in control group $[(71.8 \pm 13.6)\%]$ (P<0.01), accompanied with a sharp decline in sperm density and normal morphology rate at the same time (P<0.05), but the mean value of sperm concentration and normal morphology rate were still higher than the normal reference value of semen parameters. 3) The normal fertilization rate (70.8%), total fertilization rate (76.2%) and optimal embryo rate (50.0%) in R-ICSI group were significantly lower than those in control group (76.0%, 85.0%, 59.0%) (P<0.01). 4) Though the average number of embryo transfer in R-ICSI group (2.0 ± 0.2) was significantly higher than control group (1.9 ± 0.3) (P<0.01), the implantation rate (36.6%) was still lower than it (49.0%) (P<0.05). There were no statistical differences of clinical pregnancy rate and termination of embryo developing between the two groups (P>0.05). **Conclusion** The rate of sperm-hyaluronan binding has a certain effect on the prediction of IVF. Combined with the conventional semen parameters, the risk of fertilization failure is increasing, when the sperm-hyaluronan binding rate is lower than 63.8%, but its effect on the pregnancy is still need further study.

[Key words] Fertilization failure; Sperm-hyaluronan binding rate; Pregnancy outcome

皮下埋植避孕剂治疗子宫内膜异位症患者一年生存质量评价

柳金梅 马旭鸿 张文辉 董瑞 杜蔚云 730000 兰州, 甘肃省计划生育科学技术研究所

通信作者: 柳金梅, Tel: +86-931-8726521, Email: 1329291896@qq.com

DOI: 10.3760/cma.j.issn.2096-2716.2017.11.007

【摘要】目的 评价皮下埋植避孕剂治疗子宫内膜异位症(EMS)患者的生存质量。方法 在 60 例确诊为 EMS 的患者中,选择接受放置 II 型皮下埋植避孕剂治疗的 30 例患者纳入试验组;选择腹腔镜保守手术和接受促性腺激素释放激素激动剂(GnRH-a)治疗的 30 例患者纳入对照组,比较治疗前、治疗 6 个月和 12 个月时的疗效。结果 治疗后 6 个月,两组患者在痛经、盆腔痛、性交痛方面的疼痛均有缓解。试验组在减缓盆腔痛和性交痛方面显著优于对照组(P<0.05),对照组在减缓痛经方面显著优于试验组(P<0.05);EMS 患者生存质量调查表(EHP-5)自评分数评估结果显示,与治疗前相比,两组在治疗后均改善了相应的症状,其中试验组在情绪状态、社会支持、自我形象、完成工作、照顾孩子、性生活、医学专业人员、治疗效果、不孕等 9 个方面的效果均显著优于对照组(P<0.05)。结论 皮下埋植避孕剂能有效缓解 EMS 患者的疼痛,提高患者的生存质量。

【关键词】 皮下埋植避孕剂; 子宫内膜异位症(EMS); 生存质量

基金项目: 甘肃省卫生和计划生育委员会资助基金(GSWSKY-2014-45)

An evaluation on the life quality for endometriosis patients treated with subdermal contraceptive implant

Liu Jinmei, Ma Xuhong, Zhang Wenhui, Dong Rui, Du Weiyun

Gansu Family Planning Research Institute, Lanzhou 730000, China (Liu JM, Ma XH, Zhang WH, Dong R, Du WY)
Corresponding author: Liu Jinmei, Tel: +86-931-8726521, Email: 1329291896@qq.com

[Abstract] Objective To evaluate the life quality of one year of endometriosis (EMS) patients treated with subdermal contraceptive implant. Methods Thirty EMS patients who refused to treat surgically and were treated subdermal contraceptive implant (experimental group), while another 30 EMS patients who had undergone conservative laparoscopic surgery in laparoscopic surgery plus gonadotropin release hormone agonist (GnRH-a) group were treated as control group. Results Dysmenorrheal, pelvic pain and sexual pain were relieved in two groups after treating 6 months. The relief of pelvic pain and sexual pain of EMS patients in experimental group were significantly better than those in control group (P<0.05), but the relief of dysmenorrheal of control group was significantly better than that in experimental group (P<0.05). After treatment, the self-rated score assessed in a survery of life quality in EMS patients (EHP-5) was improved significantly as compared with that before treatment in the two groups. The emotional state, social support, self-image, completing work, care for children, sex, medical professionals, sterility and therapeutic effect of experimental group were significantly better than those in control group (P<0.05). Conclusion The pain was relieved and the life quality was improved in EMS patients treated with subdermal contraceptive implant.

[Key words] Subdermal contraceptive implant; Endometriosis (EMS); Life quality

Fund program: Medical Research Fund of Gansu Municipal Health and Family Planning Commission (GSWSKY-2014-45)

·实验研究:

香芹酚拮抗大鼠卵巢储备化疗损伤的功能

蔡静 张丹 张燕

430015 华中科技大学同济医学院附属武汉儿童医院(武汉市妇幼保健院)妇产科(蔡静、张丹); 430060 武汉大学人民医院 妇产科(张燕)

通信作者: 张燕, Tel: +86-27-88041911*82207, Email: 648434218@qq.com

DOI: 10.3760/cma.j.issn.2096-2916.2017.11.008

【摘要】目的 探索香芹酚(CAR)对注射环磷酰胺(CTX)化疗损伤后大鼠卵巢功能的影响。 方法 ①将 15 只 Fischer 344 大鼠随机分为 3 组,通过腹腔注射不同浓度 CAR(10 mg/kg、50 mg/kg、100 mg/kg)在不同 时间点利用化学发光法检测各组大鼠血清雌二醇(E_2)水平,通过酶联免疫吸附实验(ELISA)检测血清卵泡刺激 素(FSH)水平。② 64 只 Fischer 344 大鼠随机分为 4 组,分别为空白对照组、CAR 组、CTX 组和 CTX + CAR 组,每组 16 只,分别给予相应的药物后第 60 日和第 90 日,检测 E_2 和 FSH 水平,同时称量各组大鼠卵巢重量、计数卵泡数量以及卵泡直径,实时荧光定量 PCR(qPCR)检测卵巢组织雌激素受体 α (ER α)、雌激素受体 β (ER β)、孕激素受体(PR)和雄激素受体(AR)的表达。结果 50 mg/kg CAR 组能有效降低 β (0.9 ± 0.2) pg/mL]及FSH 水平[(1.3 ± 0.3) U/L],与 10 mg/kg CAR组比较有统计学意义(β -0.05),而与 100 mg/kg CAR组无统计学差异(β -0.05)。实验第 60 日质量[(38.5 ± 4.1) mg]显著低于 CTX+CAR组[(72.9 ± 5.6) mg](β -0.05),CTX组大鼠卵泡总数(1 250 ± 95)显著低于 CTX+CAR组(1 750 ± 95),差异具有统计学意义(β -0.05);此外,各组大鼠卵巢 β -2 是 β -3 是 β -3 是 β -3 是 β -4 是 β -3 是 β -4 是 β -3 是 β -4 是 β -5 是 β -6 是 β -6 是 β -6 是 β -6 是 β -7 以及 β -8 是 β -8 是 β -8 以及 β -8 是 β -8 是 β -8 以及 β -8 是 β

【关键词】 香芹酚(CAR); 卵泡刺激素(FSH); 雌二醇(E2); 卵巢肿瘤; 大鼠

基金项目: 湖北省卫生计生委重点支撑项目(WJ2017Z002)

·实验研究·

Protective effect of carvacrol on the ovarian reserve in rats receiving cyclophosphamide treatment Cai Jing, Zhang Dan, Zhang Yan

Department of Obstetrics and Gynecology, Wuhan Children's Hospital (Wuhan Maternal and Child Healthcare Hospital), Tongji Medical College, Huazhong University of Science & Technology, Wuhan 430015, China (Cai J, Zhang D); Department of Obstetrics and Gynecology, Renmin Hospital of Wuhan University, Wuhan 430060,

China (Zhang Y)

Corresponding author: Zhang Yan, Tel: +86-27-88041911*82207, Email: 648434218@qq.com

[Abstract] Objective To investigate the protective effect of carvacrol (CAR) against cyclophosphamide (CTX)-induced gonadotoxicity of ovarian reserve in rats. **Methods** Firstly, 15 Fischer344 rats were divided randomly into 3 groups (5 rats per group). Estradiol (E2) and follicle stimulating hormone (FSH) level were detected after CAR (10 mg/kg, 50 mg/kg, 100 mg/kg) intraperitoneal injection at different time points. Then, 64 Fischer344 rats were divided randomly into 4 groups (16 rats per group): control group, CAR group, CTX group and CTX+CAR group. The levels of E2 and FSH were valued at 60th and 90th day after treatment. Meanwhile, the ovarian weight, number of follicles and follicular diameter were detected at the same time. The expressions of estrogen receptor alpha (ERα), estrogen receptor beta (ERβ), progesterone receptor (PR), and androgen receptor (ER) of rat ovaries were also detected by real time PCR. Results 50 mg/kg CAR could effectively suppress the E2 and FSH level, demonstrated a statistically significance compared with the 10 mg/kg CAR group (P<0.05) and there was no statistical difference compared with the 100 mg/kg CAR group (P>0.05). E₂ and FSH levels in CTX group were significantly higher than those in CTX+CAR group (P<0.05). Meanwhile, the ovarian weight, number of follicles in CTX group were markedly lower than those in CTX+CAR group (P<0.05). Besides, there were no significant differences in mRNA expressions of $ER\alpha$, $ER\beta$, PR and AR of rat ovaries among the three groups (P>0.05). Conclusion Combination treatment with CAR could prevent CTX-induced damage to ovarian reserve probably via suppressing the E2 and FSH levels and increasing the ovarian weight, number of follicles.

[Key words] Carvacrol; Follicle stimulating hormone (FSH); Estradiol (E₂); Ovarian cancer; Rats **Fund program:** Key Projects in Pillar Program of Health Planning Commission of Hubei Province (WJ2017Z002)

·循证医学。

n-3 多不饱和脂肪酸对妊娠糖尿病患者胰岛素抵抗与妊娠结局影响的 Meta 分析

曹婧然 滑丽美 郭玉文 郭建超 华绍芳

300211 天津医科大学第二医院营养科(曹婧然、郭玉文), 内分泌科(郭建超), 产科(华绍芳); 050082 石家庄, 中国人民解放军白求恩国际和平医院营养科(滑丽美)

通信作者: 华绍芳, Tel: +86-22-88328995, Fax: +86-22-88328867, Email: hsf1974@126.com

DOI: 10.3760/cma.j.issn.2096-2916.2017.11.009

【摘要】目的 系统评价 n-3 多不饱和脂肪酸对妊娠糖尿病患者胰岛功能、血脂代谢和妊娠结局的影响。方法 检索英文数据库 Medline、EMbase、Cochrane 对照试验中心注册数据库(Cochrance Central register of controlled trials, CENTRAL), 检索语言为英语, 检索起止时间为 2000 年 1 月— 2017 年 3 月。检索词为 gestational diabetes, n-3 polyunsaturated fatty acid, clinical trial。中文数据库为中国知网,检索起止时间为 2000 年 1 月— 2017 年 3 月,检索词为妊娠糖尿病、n-3 多不饱和脂肪酸、临床研究。纳入对妊娠糖尿病患者添加n-3多不饱和脂肪酸的随机对照试验,采用Jadad量表进行研究质量评价,使用RevMan5.2软件进行Meta分析。结果 最终纳入 5 篇英文文献,来源于 2 个不同国家的高质量研究。n-3 组的胰岛素释放(I^2 =92%, 95% CI=-4.95~-1.03, Z=2.99, P=0.003),新生儿高胆红素血症的发病率(I^2 =0%, 95% CI=0.07~0.58, Z=2.94, P=0.003),n-3 组新生儿住院率低于对照组(I^2 =0%, 95% CI=0.07~0.64, Z=2.78, P=0.005),n-3 组的血清总胆固醇高于对照组(I^2 =82%, 95% CI=2.39~10.61, Z=3.1, P=0.002),差异均有统计学意义。空腹血糖(FPG)(I^2 =100%, 95% CI=-9.87~16.98, Z=0.52, P=0.6)、血清甘油三酯(I^2 =99%, 95% CI=-40.69~20.85, Z=0.63, P=0.53)、需要接受胰岛素治疗的比例(I^2 =0%, 95% CI=0.05~2.16, Z=1.16, Z=0.25)和巨大儿比例(Z=9%, 95% Z=0.11~1.45, Z=1.38, Z=0.17)组间差异均无统计学意义。结论 现有临床证据不足以证明 n-3 脂肪酸对改善妊娠糖尿病患者胰岛素抵抗和母代妊娠结局有益,但对新生儿健康状况有益作用。

【关键词】 n-3 多不饱和脂肪酸; 妊娠糖尿病; 胰岛素抵抗(IR); 妊娠结局; Meta 分析 基金项目: 河北省医学科学研究重点课题(20170203)

·循证医学 ·

Effect of n-3 ployunsaturated fatty acid on insulin resistance and the pregnancy outcome of gestational diabetes — a Meta analysis Cao Jingran, Hua Limei, Guo Yuwen, Guo Jianchao, Hua Shaofang Department of Nutrition (Cao JR, Guo YW), Endocrinology Department (Guo JC), Obstetrical Department (Hua SF), the Second Hospital of Tianjin Medical University, Tianjin 300211, China; Department of Nutrition, Bethune International Peace Hospital, Shijiazhuang 050082, China (Hua LM)

Corresponding author: Hua Shaofang, Tel: +86-22-88328995, Fax: +86-22-88328867, Email: hsf1974@126.com [Abstract] Objective To systematically evaluate the effect of n-3 ployunsaturated fatty acid on insulin resistance, blood fat and the pregnancy outcome of gestational diabetes. **Methods** Databases of Medline, EMBase, Cochrane Central register of controlled trials (CENTRAL) were retrieved, and the language was English. Database of CNKI was retrieved, and the language was Chinese. Time was from January 2000 to March 2017, the search words were gestational diabetes, n-3 polyunsaturated fatty acid, clinical trial. All the randomized controlled trials were included after assessed by Jadad scale. RevMan 5.2 was used for statistical analysis. Results There were 5 English literatures that came from 2 different countries at last. The level of insulin (I^2 =92%, 95% CI=-4.95--1.03, Z=2.99, P=0.003), newborns' hyperbilirubinemia rate (I=0%, 95% CI=0.07-0.58, Z=2.94, P=0.003), newborns' hospitalization rate $(I^2=0\%, 95\% CI=0.07-0.64, Z=2.78, P=0.005)$ in n-3 group were lower than those in control group, total cholesterol (F=82%, 95% CI=2.39-10.61, Z=3.1, P=0.002) in n-3 group was higher than that in control group, the difference was statistically significant. There were no statistical difference in FPG (I²=100%, 95% CI=-9.87-16.98, Z=0.52, P=0.6), triglycerides ($I^2=99\%$, 95% CI=-40.69-20.85, Z=0.63, P=0.53), need to insulin therapy after intervention rate (F=0%, 95% CI= 0.05-2.16, Z=1.16, P=0.25) and the ratio of macrosomia >4 000 g (F=9%, 95% CI=0.11-1.45, Z=1.38, P=0.17). Conclusion The available clinical evidence is insufficient to prove that n-3 fatty acid is beneficial to improve the insulin resistance and the pregnancy outcome of pregnant, but it is beneficial to neonatal health.

【Key words】 n-3 polyunsaturated fatty acids; Gestational diabetes; Insulin resistance; Pregnancy outcome; Meta analysis

Fund program: Key Project of Hebei Medical Scientific Research (20170203)

·临床报道。

贵州六盘水市彝族与汉族女性叶酸代谢关键酶基因多态性特征分布

王辉 鲁衍强 王宏 田艳 胡秀颀 涂传荧 彭秋菊 杨琦 553000 六盘水市妇幼保健院(王辉、田艳、胡秀颀、涂传荧、彭秋菊); 200433 上海靶向分子医学研究所(鲁衍强、王宏); 100101 北京, 中国疾病预防控制中心妇幼保健中心(杨琦) 通信作者: 王宏, Tel: +86-18930996981/18019184001, Email: wanghong@genechina.com DOI: 10.3760/cma.j.issn.2096-2916.2017.11.010

【摘要】目的 了解六盘水市彝族、汉族育龄女性叶酸代谢水平,为指导当地孕期叶酸补充提供一定的依据。方法 选取 2016—2017 年期间进行孕期体检的育龄女性 1 054 例(汉族 950 例,彝族 104 例)为研究对象,采集口腔黏膜上皮脱落细胞提取基因组 DNA,利用荧光定量 PCR 方法检测受检者 5,10-亚甲基四氢叶酸还原酶(MTHFR)(C677T、A1298C)和甲硫氨酸合成酶还原酶(MTRR)(A66G)位点基因型与等位基因频率,并通过与西南地区已报道的其他少数民族进行比较,获得本地区彝族、汉族上述基因位点多态性分布特征。结果 六盘水市彝族女性 MTHFR C677T 位点基因型和等位基因频率与当地汉族、思南苗族、思南土家族、大理白族比较均具有统计学差异,其中 MTHFR 677CT,677TT 基因型频率均低于其他民族。结论 六盘水市彝族与汉族育龄女性叶酸代谢关键酶基因位点多态性特征有所区别,可以有针对性地制定符合当地民族特征的个性化叶酸补充方案。

【关键词】 六盘水彝族; 六盘水汉族; 5,10- 亚甲基四氢叶酸还原酶(MTHFR); 甲硫氨酸合成酶还原酶 (MTRR)

基金项目: 中国疾病预防控制中心妇幼保健中心妇幼保健分子遗传医学研究专项计划(FY-ZX-ZD-0313)

· 临床报道 ·

SNP polymorphism of key enzymes in folic acid metabolism in Yi and Han women in Liupanshui City Guizhou Province Wang Hui, Lu Yanqiang, Wang Hong, Tian Yan, Hu Xiuqi, Tu Chuanying, Peng Qiuju, Yang Qi

Liupanshui Maternal and Child Health Care Hospital, Liupanshui 553000, China (Wang H, Tian Y, Hu XQ, Tu CY, Peng QJ); Institute of Therapy and Molecular Medicine, Shanghai 200433, China (Lu YQ, Wang H); National Center for Women and Children's Health, Chinese CDC, Beijing 100101, China (Yang Q) Corresponding author: Wang Hong, Tel: +86-18930996981/18019184001, Email: wanghong@genechina.com

[Abstract] Objective To study the metabolism level of folic acid between Yi and Han women in Liupanshui, and to guide supplement of folic acid. **Methods** Totally 1 054 fertile women were selected including 104 Yi women and 950 Han women. Genomic DNA was obtained from the oral mucosa cells. Genetype and allele frequency of 5,10-methylenetetrahydrofolate reductase (*MTHFR*) (C677T, A1298C) and methionine synthase reductase (*MTRR*) (A66G) were detected by Taqman-MGB technology. Genetype and allele frequency were compared with other ethnic minorities women in China Southwest which have been reported before. **Results** Genetype and allele frequency of *MTHFR* C677T in Liupanshui Yi women were different from Liupanshui Han and other minorities (Sinan Miao women, Sinan Tujia women, Dali Bai women). *MTHFR* 677CT/677TT genetype frequency in Liupanshui Yi women were lower than that in Han and others minorities, which could guide for a more individualized folic acid supplement program for different ethnic women.

[Key words] Liupanshui Yi women; Liupanshui Han women; 5,10-Methylenetetrahydrofolate reductase (MTHFR); Methionine synthase reductase (MTRR)

Fund program: Special Project of Molecular Genetic Medicine for Maternal and Child Health Care in Maternal and Child Health Center of Chinese Center for Disease Control and Prevention (FY-ZX-ZD-0313)

·出生缺陷专栏。

质谱技术检测羊水代谢物对丙酸血症进行产前诊断

韩凤 鄂慧姝 韩连书 季文君 徐烽 叶军 邱文娟 张惠文 顾学范 200092 上海交通大学医学院附属新华医院内分泌 / 遗传科, 上海市儿科医学研究所 通信作者: 韩连书, Tel: +86-13818170919, Email: hanlianshunls@xinhuamed163.com.cn DOI: 10.3760/cma.j.issn.2096-2916.2017.11.011

【摘要】目的 探讨串联质谱及气相色谱质谱技术检测羊水中的酰基肉碱及有机酸用于丙酸血症 (propionic acidemia, PA)产前诊断的诊断价值。方法 收集 2010 年—2016 年 40 例于上海交通大学医学院附属新华医院进行产前诊断且生育过 PA 患儿的孕妇作为 PA 母亲组。从同期进行常规产前诊断孕妇中随机选取 40 例作为对照组。2 组孕妇均于妊娠 16~20 周进行羊膜腔穿刺术抽取羊水。采用串联质谱检测羊水丙酰肉碱(propionylcarnitine, C3)、乙酰肉碱(acetylcarnitine, C2)水平,采用气相色谱质谱检测羊水甲基枸橼酸、3-羟基丙酸水平,部分羊水细胞进行基因检测。结果 PA 母亲组 4 例孕妇羊水 C3[9.53(6.06~11.45) μmol/L]、C3/C2[1.03(0.62~1.43)]、甲基枸橼酸[3.15(2.05~4.58) mmol/mol 肌酐]水平均高于对照组[1.14(0.52~3.40) μmol/L, 0.11(0.05~0.22), 0.00(0.00~0.34) mmol/mol 肌酐],提示胎儿为PA 阳性患儿,检出率为10%;其中3 例进行了基因突变检测均检测到突变位点。3-羟基丙酸在对照组与阳性组之间差异无统计学意义。结论 PA 孕妇再生 PA 患儿的几率为 10% 左右,可利用串联质谱及气相色谱质谱技术检测羊水中的 C3、甲基枸橼酸水平,对先证者为 PA 的孕妇进行产前诊断。

【关键词】 串联质谱; 气相色谱质谱; 产前诊断; 丙酸血症(PA) 基金项目: 国家重点研发计划(2016YFC0901505)

· 出生缺陷专栏 ·

Prenatal diagnosis of propionic acidemia by amniotic fluid metabolites analysis using mass spectrometry

Han Feng, E Huishu, Han Lianshu, Ji Wenjun, Xu Feng, Ye Jun, Qiu Wenjuan, Zhang Huiwen, Gu Xuefan Department of Pediatric Endocrinology and Genetic, Xinhua Hospital, Shanghai Institute for Pediatric Research, Shanghai Jiao Tong University School of Medicine, Shanghai 200092, China (Han F, E HS, Han LS, Ji WJ, Xu F, Ye J, Qiu WJ, Zhang HW, Gu XF)

Corresponding author: Han Lianshu, Tel: +86-13818170919, Email: hanlianshunls@xinhuamed163.com.cn

[Abstract] Objective To investigate the value of acylcarnitine and organic acid in amniotic fluid for the diagnosis of propionic acidemia (PA) by tandem mass spectrometry and gas chromatography-mass spectrometry (GC-MS). **Methods** From 2010 to 2016, 40 pregnant women with PA neonate received pregnatal diagnosis of PA in Xinhua Hospital of Shanghai Jiao Tong University School of Medicine (as PA mother group). Another 40 cases of pregnant women for conventional prenatal diagnosis at the same period were collected as control group. The pregnant women of two groups had the amniocentesis at 16–20 weeks of gestation. The levels of propionylcarnitine (C3) and acetylcarnitine (C2) in amniotic fluid were detected by tandem mass spectrometry, and the levels of methylcitrate acid and 3-hydroxypropionate were determined by gas chromatography-mass spectrometry. Part of the amniotic fluid cells were made genetic testing. **Results** In PA mother group, 4 fetuses were positive and the detection rate was 10%. The levels of C3 [9.53 (6.06–11.45) μmol/L], C3/C2 [1.03 (0.62–1.43)] and methylcitrate acid [3.15 (2.05–4.58) mmol/molCr] in amniotic fluid of these 4 cases were higher than those in control group [1.14 (0.52~3.40) μmol/L,

0.11 (0.05–0.22), 0.00 (0.00–0.34) mmol/molCr]. Three cases of the PA-positive children were diagnosed by gene testing. There was no significant difference of 3-hydroxypropionic acid between control group and the positive group. **Conclusion** For pregnant women with PA proband, the probability of children regeneration with PA is about 10%. Tandem mass spectrometry and gas chromatography-mass spectrometry can be used to detect the levels of C3 and methylcitrate in amniotic fluid, and to make prenatal diagnosis of PA.

[Key words] Tandem mass spectrometry; Gas chromatography-mass spectrometry; Prenatal diagnosis; Propionic acidemia (PA)

Fund program: The National Key Research and Development Program of China (2016YFC0901505)

•出生缺陷专栏 •

高通量测序技术鉴定新生儿窒息性胸廓发育不良症1例

王莹 李晓梅 杨小萌 张开慧 刘毅 盖中涛

250022 济南, 山东大学齐鲁儿童医院儿研所(王莹、杨小萌、张开慧、刘毅、盖中涛), 新生儿科(李晓梅、盖中涛)

通信作者: 刘毅, Tel: +86-18866115987, Fax: +86-531-87964257, Email: liuyi-ly@126.com 前 2 位作者对本文有同等贡献, 均为第一作者

DOI: 10.3760/cma.j.issn.2096-2916.2017.11.012

【摘要】目的 对 1 例多器官发育缺陷的新生儿进行高通量全外显子组测序(WES),明确遗传学病因。方法 对患儿进行临床检查,采集患儿及其父母外周静脉血,进行全外显子组基因测序与分析,再对可疑突变位点进行 Sanger 测序验证。结果 患儿临床表现为胸廓发育畸形伴先天性心脏病和肝脾肿大,全外显子组测序显示其存在 *DYNC*2H1 基因 c.8512C>T(p.R2838*)及 c.10163C>T(p.P3388L)复合杂合突变,分别遗传自父亲和母亲。结论 根据测序结果结合临床表现,鉴定该患儿为 *DYNC*2H1 基因复合杂合突变引起的窒息性胸廓发育不良(ATD)。

【关键词】 窒息性胸廓发育不良(ATD); 先天性心脏病; DYNC2H1; 全外显子组测序(WES) 基金项目: 山东省科技计划项目资助(2013GSF11829)

• 出生缺陷专栏 •

Identification of an asphyxiating thoracic dysplasia in a neonate by high throughput sequencing

Wang Ying, Li Xiaomei, Yang Xiaomeng, Zhang Kaihui, Liu Yi, Gai Zhongtao

Pediatric Research Institute (Wang Y, Yang XM, Zhang KH, Liu Y, Gai ZT), Neonatal Department (Li XM, Gai ZT),

Qilu Children's Hospital of Shandong University, Jinan 250022, China

Corresponding author: Liu Yi, Tel: +86-18866115987, Fax: +86-531-8796425, Email: liuyi-ly@126.com

Wang Ying and Li Xiaomei are the first authors who contributed equally to the article

(Abstract) Objective To investigate the genetic cause of a neonatal with multi-organs defects by using high throughput whole exome sequencing (WES). Methods The patient was clinical examined and the peripheral venous blood were collected from the patient and her parents. Whole exome sequencing was performed to analyze her genetic cause. The likely pathogenic mutations were validated by Sanger sequencing. Results Clinical manifestation of the patient displayed that she had thoracic malformation, congenital heart disease and hepatosplenomegaly. WES result showed that the patient carried the compound heterozygous mutations of c.8512C>T (p.R2838*) and c.10163C>T (p.P3388L) in *DYNC*2H1 gene which were inherited from her father and mother, individually. **Conclusion** Based on the WES results and clinical features, the neonate suffered from asphyxiating thoracic dystrophy (ATD) caused by *DYNC*2H1 mutation.

[Key words] Asphyxiating thoracic dystrophy; Congenital heart disease; DYNC2H1; Whole exome sequencing

Fund program: Science and Technology Project of Shandong Province (2013GSF11829)

·现场调查。

高校学生的生育意识现状调查分析

宋晓艳 罗阳

410013 中南大学湘雅护理学院

通信作者: 罗阳, Tel: +86-731-82650269, Email: 92375347@qq.com

DOI: 10.3760/cma.j.issn.2096-2916.2017.11.013

【摘要】目的 了解湖南省大学生的生育意识现状,为相关政府部门和高校制定性教育计划提供依据。方法 采用分层随机抽样的方法,在湖南省 3 所综合性大学抽取 1 100 名大学生进行生育意识问卷调查,主要包括生育意愿、生育问题意识、生育知识来源途径、不孕不育情况下的行为选择等内容。结果 问卷回收率为93%,大学生预期生育第一个和最后一个孩子的平均年龄分别为(28.6±1.8)岁和(35.1±3.8)岁。86.4% 大学生对生育力开始下降的年龄不甚清楚,74.3% 的大学生高估了体外受精(IVF)的成功率,90% 的大学生想在未来要 1~2 个孩子,5% 的大学生在未来不想生育孩子;对于拥有孩子的重要性,大学生的评分平均为 8 分(评分范围为 0~10 分);57% 的大学生通过互联网获取生育知识。结论 大学生基于对女性生育力的错误认知,做出延迟生育的决定可能会增加未来不孕不育的风险,导致非自愿无子女的发生。

【关键词】 生育意识; 生育力; 延迟生育; 体外受精(IVF); 大学生

·现场调查。

Investigation and analysis of college students' fertility awareness Song Xiaoyan, Luo Yang Xiang Ya School of Nursing, Central South University, Xiangya 410013, China (Song XY, Luo Y) Corresponding author: Luo Yang, Tel: +86-13548736639, Email: 492375347@qq.com

[Abstract] Objective To understand the current situation of college students' fertility awareness in Hunan province, then provide the basis for the related government departments and universities to develop sexual education programs. **Methods** Using stratified random sampling method, 1 100 college students from three comprehensive universities in Hunan province were surveyed with fertility awareness questionnaire which mainly includes the fertility desire, the fertility awareness, the source of fertility knowledge and the behavior choice under the condition of infertility. **Results** The average recovery rate was 93%, and the expected average ages of college students when they have the first and last child were (28.6 ± 1.8) years old and (35.1 ± 3.8) years old. About 86.4% college students overestimate the age when fertility begins to decline, 74.3% college students overestimate the success rate of *in vitro* fertilization (IVF), 90% college students want to have 1–2 children in the future, 5% college students don't want to have children in the future; for the importance of having children, college students give 8 points (range from 0 to 10); 57% college students get fertility knowledge through the internet. **Conclusion** Based on the misunderstanding of women's fertility, the decision to delay childbearing may increase the risk of infertility in the future, and result in involuntary absence of children.

Key words Fertility awareness; Fertility; Delayed childbearing; *In vitro* fertilization (IVF); College students

· 生殖伦理 ·

国内首例冻融胚胎移植纠纷案的伦理与法律考量

曹文丽 姜雯 叶飞君 夏邦世 周伟文 316004 舟山市妇幼保健院生殖医学中心

通信作者: 曹文丽, Tel: +86-580-2065552, Fax: +86-580-2065222, Email: cwl1968hjn@sina.com DOI: 10.3760/cma.j.issn.2096-2916.2017.11.014

【摘要】舟山冻融胚胎移植纠纷诉讼一案引发社会各界极大的关注和讨论。不仅创下浙江省乃至全国司法实践中同类案例的第一个成功记录,焦点更在于冷冻胚胎能否作为遗产被继承、给类似的"单身女性"继续实施辅助生殖技术是否违背法规、有无影响到将来孩子的成长等法律和伦理问题。本文从该案例判决的争议焦点出发,综合国内外相关的法规、案例来探讨一方去世后冷冻胚胎的归属权和处置问题,并认为在不违反公序良俗的前提下,死者家属应享有对冷冻胚胎的处置权和生育权,体现了社会法制的进步,医院人文的关怀,给伦理学带来了实践示范意义。

【关键词】 冷冻胚胎; 继承; 移植; 法律; 伦理

• 生殖伦理•

Ethical and legal considerations on the first domestic of frozen embryo-thawed transfer in China Cao Wenli,

Jiang Wen, Ye Feijun, Xia Bangshi, Zhou Weiwen

Department of Reproductive Center, Zhoushan Maternity and Child Healthcare Hospital, Zhoushan 316004, China (Cao WL, Jiang W, Ye FJ, Xia BS, Zhou WW)

Corresponding author: Cao Wenli, Tel: +86-580-2065552, Fax: +86-580-2065222, Email: cwl1968hjn@sina.com

[Abstract] Zhoushan frozen-thawed embryo transfer dispute lawsuit case caused a lot of attention. It is the first successful record not only in Zhejiang province but also the whole country of similar cases in the judicial practice, The focus on frozen embryos can be inherited as a legacy, it is legal or not to implement the assisted reproductive technology for similar singal women, it has any influence to the growth of children in the future. This paper which based on the focus of the case judgment and the related laws and regulations will discuss the ownership and disposal problems after the death of husband or wife. The families of the dead should enjoy the right of disposition of frozen embryos and fertility without violating the premise. It embodies the progress of social legal system, the hospital humanistic care and brings practice demonstration significance.

[Key words] Frozen embryos; Inherit; Transplant; Law; Ethics

· 综述·

卵巢衰老与线粒体相关的研究进展

田海丽 李蓉

200030 上海交通大学医学院附属国际和平妇幼保健院

通信作者: 李蓉, Tel: +86-18017310170, Email: lrivf@163.com

DOI: 10.3760/cma.j.issn.2096-2916.2017.11.015

【摘要】 伴随生育年龄推迟及全面开放"二孩"政策,有生育需求的高龄女性显著增多。而与其他器官相比,卵巢最易受年龄的影响。女性年龄相关的卵母细胞数量减少和质量下降共同决定了卵巢衰老。线粒体与卵胞质成熟密切相关,是卵巢衰老的决定要素。进一步了解线粒体与卵巢衰老的关系及探索改善卵母细胞质量的可能措施,将有助于为高龄女性提供更好的治疗策略,提高高龄女性的妊娠率。

【关键词】 线粒体; 线粒体 DNA(mtDNA); 卵母细胞; 卵巢衰老

基金项目: 上海市自然科学基金(14ZR1443900)

Advance research of ovarian aging associated with mitochondria Tian Haili, Li Rong

The International Peace Maternity and Child Health Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai 200030, China (Tian HL, Li R)

Corresponding author: Li Rong, Tel: +86-18017310170, Email: lrivf@163.com

[Abstract] With the postponement of childbearing age and the universal of the "two children" policy, there is a significant increase in the number of advance aged women with fertility needs. Compared with other organs, ovaries are most susceptible to age. Age-related reduction in the number of oocytes and the decline in oocyte quality consistently determine ovarian aging. Mitochondria is the decisive factor in ovarian aging, closely related to oocyte maturation. To further understand the relationship between mitochondria and ovarian aging and to explore the possible measures to improve the quality of oocytes will help to provide better treatment strategies for advance aged women and improve the rate of pregnancy in older women.

Key words Mitochondria; Mitochondrial DNA (mtDNA); Oocytes; Ovarian aging

Fund program: Shanghai Natural Science Foundation of China (14ZR1443900)

· 综述·

母-胎界面巨噬细胞作用的研究进展

丁锦丽 尹太郎 杨菁

430060 武汉大学人民医院生殖医学中心(丁锦丽、尹太郎、杨菁); 430060 武汉, 湖北省辅助 生殖与胚胎发育医学临床研究中心(丁锦丽、尹太郎、杨菁)

通信作者: 杨菁, Tel: +86-27-8804191, Email: dryangqing@hotmail.com

DOI: 10.3760/cma.j.issn.2096-2916.2017.11.016

【摘要】 巨噬细胞是母 - 胎界面第二大类白细胞,在宿主防御、血管生成、免疫调节和组织重构方面发挥重要作用。母 - 胎界面异常激活的巨噬细胞会影响滋养层细胞功能以及胎盘发育,引发早产、先兆子痫等妊娠并发症。本文就母 - 胎界面巨噬细胞的特点及其在正常妊娠和病理妊娠中的研究进展进行综述。

【关键词】 蜕膜巨噬细胞; 妊娠; 滋养层细胞; 螺旋动脉重塑

基金项目: 国家自然科学基金(81771618, 81771662)

Research progress on the function of macrophages at the fetal-maternal interface Ding Jinli, Yi Tailang, Yang Jing

Reproductive Medical Center, Renmin Hospital of Wuhan University, Wuhan 430060, China (Ding JL, Yi TL, Yang J); Hubei Clinic Research Center for Assisted Reproductive Technology and Embryonic Development, Wuhan 430060, China (Ding JL, Yi TL, Yang J)

Corresponding author: Yang Jing, Tel: +86-27-8804191, Email: dryangqing@hotmail.com

【Abstract】 Macrophages are the second most abundant leukocyte population at the fetal-maternal interface, which perform many specific functions including host defense, angiogenesis, immunological regulation, and tissue development. Aberrantly activated uterine macrophages can affect trophoblast function and placental development, which may result in various adverse pregnancy outcomes, including pre-eclampsia and premature labor. In this review, we will focus on the characteristic of macrophages at the fetal-maternal interface, and those roles in normal and pathological pregnancy.

[Key words] Decidual macrophages; Pregnancy; Trophoblast; Spiral artery remodeling **Fund program**: National Natural Science Foundation of China (81771618, 81771662)

Treg/Th17在不明原因复发性流产中的作用机制

钱金凤 李大金 王凌

200011 复旦大学上海医学院附属妇产科医院暨妇产科研究所,复旦大学中西医结合研究院 妇产科研究所,上海市女性生殖内分泌相关疾病重点实验室

通信作者: 王凌, Tel: +86-18221815182, Fax: +86-21-63450944, Email: dr.wangling@fudan.edu.cn DOI: 10.3760/cma.j.issn.2096-2916.2017.11.017

【摘要】妊娠是一个复杂的生理过程, 母-胎免疫失衡与不明原因复发性流产等多种妊娠并发症有关。在母-胎界面, 介导免疫耐受的调节性 T 细胞(Treg)和具有促炎作用的 Th17 细胞, 起源上有同源性, 功能上可能互相拮抗, 在一定条件下可相互转化, 其表达失衡可能和不明原因复发性流产有关。本文就 Treg、Th17 细胞在不明原因复发性流产中的作用机制作一综述。

【关键词】调节性 T 细胞(Treg); Th17 细胞; 复发性流产; 免疫耐受

基金项目: 国家自然科学基金(31571196, 30801502); 上海市医学引导类项目(15401932200); 上海市高峰学科(中西医结合)建设项目(20150407); 上海市浦江人才计划(11PJ1401900)

Mechanism of Treg/Th17 in unexplained recurrent spontaneous abortion Qian Jinfeng, Li Dajin, Wang Ling Obstetrics and Gynecology Hospital of Fudan University, the Academy of Integrative Medicine of Fudan University, Shanghai Key Laboratory of Female Reproductive Endocrine-related Diseases, Shanghai 200011, China (Qian JF, Li DJ, Wang L)

Corresponding author: Wang Ling, Tel: +86-18221815182, Fax: +86-21-63450944, Email: dr.wangling@fudan.edu.cn

[Abstract] Pregnancy is a complicated physiological process and the growth and development of fetus in the uterine depend on immunological modulation in maternal-fetal interface. Regulatiry T cells (Treg) usually mediate immunological tolerance and Th17 cells often act as proinflammatory cells. Treg and Th17 cells are homologous in origin and antagonistic in function. Under certain circumstances, Treg cells are able to transdifferentiate into Th17 cells and vice versa. The imbalance of Treg/Th17 may be associated with unexplained recurrent spontaneous abortion (URSA). So we here summarize the recent advances of Treg/Th17 in URSA.

[Key words] Regulatory T cell (Treg); Th17 cell; Recurrent spontaneous abortion; Immunological tolerance **Fund program**: the National Natural Science Fundation of China (31571196, 30801502); the Science and Technology Commission of Shanghai Municipality YIXUEYINGDAO Project (15401932200); Development Project of Shanghai Peak Disciplines-Integrative Medicine (20150407); the Shanghai Pujiang Program (11PJ1401900)

雄激素不敏感综合征雄激素受体基因突变的研究现状

马若鹜 谢梅青

510235 广州, 中山大学孙逸仙纪念医院

通信作者: 谢梅青, Tel: +86-18922182801, Fax: +86-20-81332573, Email: mqxiegz@163.com

DOI: 10.3760/cma.j.issn.2096-2916.2017.11.018

【摘要】目前已报道的与雄激素不敏感综合征(AIS)有关的雄激素受体(AR)基因突变超过500个,95%的完全型AIS(CAIS)携带有AR突变基因。部分型AIS(PAIS)检测显示AR突变基因的比例占28%,同一基因型患者性别的养成和雄性化程度存在很大差异,辅助活化因子及第1外显子CAG重复数量差异被认为是造成表型差异的原因。轻型AIS(MAIS)相关的AR基因突变有44个,大部分患者出生时具有正常男性表型,仅仅表现为不育。第1外显子是MAIS突变热区,CAG重复数目超过正常可引起轻微的雄激素抵抗及生育力下降。本文就3种类型AIS相关的AR基因突变研究进展进行综述。

【关键词】 雄激素不敏感综合征(AIS); 受体; 突变; 雄性化程度

Research progress of androgen receptor gene mutation related to androgen insensitivity syndrome

Ma Ruowu, Xie Meiqing

Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou 510235, China (Ma RW, Xie MQ) Corresponding author: Xie Meiqing, Tel: +86-18922182801, Fax: +86-20-81332573, Email: mqxiegz@163.com

[Abstract] It was reported that more than 500 androgen receptor (AR) gene mutations were related to androgen insensitivity syndrome (AIS). AR gene mutation is detected about 95% of the conplete AIS (CAIS) patient, and 28% of the partial AIS (PAIS). The masculinization varies a lot even with the same genotype, which may due to the auxillary activating factor and CAG repeats of the first exon. Forty-four muations are detected in the MAIS patient, most of them show normal phenotype with infertility. The first exon has been the hotspot region. The abnormal increased CAG repeats may lead to androgen resistence and decresaed fertility in those patients. Study progress on 3 types of AR gene mutation related to AIS was summarized in the article.

[Key words] Androgen insensitivity syndrome (AIS); Receptor; Mutation; Masculinization