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中国超重/肥胖不孕不育患者体质量管理路径与流程专家共识

中国超重/肥胖不孕不育患者体质量管理路径与流程专家共识编写组

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【摘要】 近年来,国际上对超重/肥胖患者已经形成了一些综合医疗管理的指南和共识,然而对超重/肥胖不孕不育患者的体质量管理尚无具体的管理路径和流程。因此,为更好地对超重/肥胖不孕不育患者进行孕前干预,改善妊娠结局,降低剖宫产率和减少产后体质量滞留,国内相关专家结合国内外的诸多证据起草了我国首个不孕不育患者体质量管理路径与流程专家共识。此共识能进一步规范超重/肥胖不孕不育患者体质量管理路径,设立标准化体质量管理工作流程,使超重/肥胖不孕不育患者体质量管理更加科学,便于更多的临床专业人员及医疗保健人员掌握和使用,更好地为患者服务。

【关键词】 肥胖; 超重; 不孕不育; 体质量

Expert consensus on the weight management of overweight/obese infertility patients in China

Chinese Experts Consensus Group on the Body Quality Management Approach and Process for Overweight/Obese Infertility Patients

Corresponding author: Zhang Xuehong, Email: zhangxueh@lzu.edu.cn, Tel: +86-931-8357358

【Abstract】 In recent years, there has been some international consensus on the integrated medical management of overweight/obesity. However, there is no specific management path and process for the management of overweight/obesity infertile patients. In order to take better pre-pregnancy

intervention for patients with infertility and overweight/obesity, improve pregnancy outcomes, reduce cesarean section rates and reduce postpartum weight retention, experts from relevant field drafted the first infertility patient weight management path and process expert consensus based on evidence. We hope the consensus will further standardize the weight management pathway for patients with infertility and overweight/obesity, establish a standardized weight management workflow to make the weight management of overweight/obese infertile patients more scientific. In the same time, more professionals and health care personnel can use it in clinic, providing better service for patients.

【Key words】 Obesity; Overweight; Infertility; Body weight

· 规范与标准 ·

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合并子宫体良性疾病的早期人工流产专家共识

中华医学会计划生育学分会

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【摘要】 本共识主要针对合并子宫肌瘤、子宫腺肌病、子宫内膜息肉及子宫内膜无不典型增生等子宫体良性疾病的14周前人工流产,从人工流产术前风险评估及预案、人工流产方法选择及并发症处理、人工流产同时行子宫体良性疾病手术的决策及方法、人工流产后避孕方法的选择等方面深入讨论,希望能加强合并子宫体良性疾病的早期人工流产的规范管理,保证手术安全。

【关键词】 子宫体良性疾病; 人工流产; 共识

Expert consensus on early induced abortion with benign diseases of the uterus

Family Planning Branch of Chinese Medical Association

Corresponding author: Gu Xiangying, Email: gxy6283@163.com

【Abstract】 This consensus mainly aimed at induced abortions before 14 weeks of benign diseases of the uterus, such as uterine fibroids, adenomyosis, endometrial polyps, and no dysplasia of the endometrium. The report decision from the preoperative risk assessment, pre-plans, methods of induced abortion,

treatment of complications and decision-making and methods for induced abortion and surgery for benign diseases of the uterus, selection of contraceptive methods after induced abortion. We hope to strengthen the standardized management of early induced abortion with benign diseases of the uterus and ensure the operation Safety.

【Key words】 Benign diseases of the uterus; Induced abortion; Consensus

·临床研究·

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早卵泡期长效长方案和拮抗剂方案 在预期卵巢高反应患者中的应用比 较及自身对照研究

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【摘要】 目的 探讨早卵泡期长效长方案（长长方案）和拮抗剂方案在预期卵巢高反应患者中的临床应用。方法 回顾性队列研究分析 2015 年 9 月至 2019 年 5 月期间在郑州大学第三附属医院生殖中心行体外受精/卵胞质内单精子注射-胚胎移植（IVF/ICSI-ET）的预期卵巢高反应患者共 2575 个周期的临床资料，其中长长方案组 1855 个周期，拮抗剂方案组 720 个周期，比较两组患者的临床和实验室指标、全部胚胎冷冻第一周期移植的妊娠结局、每取卵周期的累积妊娠率及首次 IVF/ICSI 助孕周期妊娠所需时间（TTP）；并采用自身对照研究回顾性分析其中前次行长长方案助孕再次拮抗剂方案助孕周期的临床资料及前次行长长方案助孕再次行长长方案助孕周期的临床资料。结果 ①两组患者的年龄、体质量指数（BMI）、基础卵泡刺激素（bFSH）、抗苗勒管激素（AMH）、人绒毛膜促性腺激素（hCG）注射日内膜厚度差异均无统计学意义（ $P>0.05$ ）。长长方案组促性腺激素（Gn）启动量〔 135.11 ± 36.61 ）IU〕、获卵数〔 17.79 ± 7.80 ）枚〕、可利用胚胎数〔 9.08 ± 5.56 ）

枚]、优质胚胎数[(5.18±4.56)枚]明显低于拮抗剂组[(170.12±53.94) IU、(20.60±9.92)枚、(10.96±6.59)枚、(6.47±4.97)枚] ($P<0.001$ 、 $P<0.001$ 、 $P<0.001$ 、 $P=0.012$) ;而 Gn 使用时间[(14.3±3.23) d]、Gn 使用总量[(2322.08±1020.48) IU]、中重度卵巢过度刺激综合征 (OHSS) 发生率 (9.54%)、hCG 扳机后中重度 OHSS 发生率 (9.54%)、新鲜周期临床妊娠率 (69.44%) 明显高于拮抗剂组 [(9.97±2.47) d、(1884.19±774.16) IU、0.83%、3.95%、53.94% , P 均 <0.001]。②全部胚胎冷冻第一周期移植的临床妊娠率和流产率两组比较差异无统计学意义 ($P>0.05$)。③两组患者累积妊娠率比较差异无统计学意义 ($P>0.05$) ;拮抗剂组新鲜周期移植后妊娠和冷冻胚胎周期移植后妊娠的周期 TTP [(47.67±3.18) d、(140.33±45.43) d]要明显少于长长方案组[(81.25±3.72) d、(185.19±46.52) d , P 均 <0.001] , 但总移植周期 TTP 两组比较差异无统计学意义 ($P>0.05$)。④长长方案和拮抗剂方案自身对照的比较显示 : 长长方案组可利用胚胎数 [(5.79±3.14) 枚]、优质胚胎数 [(2.78±1.50) 枚]明显低于拮抗剂组 [(10.14±4.74) 枚、(5.70±3.50) 枚] ($P=0.027$ 、 $P=0.005$) , 而 Gn 使用总量 [(2535.80±1212.17) IU]、中重度 OHSS 发生率 (4.55%) 明显高于拮抗剂组 [(2075.28±856.03) IU、0] ($P=0.049$ 、 $P=0.043$)。⑤长长方案助孕和再次长长方案自身对照的比较显示 : 再次长长方案助孕的 BMI [(24.63±2.99) kg/m^2] 小于第一周期长长方案者 [(25.01±3.12) kg/m^2 , $P=0.049$] , 而优质胚胎数 [(4.00±3.58) 枚]和临床妊娠率 (52.10%) 明显高于第一周期长长方案者 [(2.56±2.12) 枚、29.41%] ($P=0.046$ 、 $P=0.004$)。结论 对于预期卵巢高反应的患者,拮抗剂方案可显著降低促排卵时间、促排卵剂量、中重度 OHSS 发生率,提高获卵数、可利用胚胎数及优质胚胎数,但新鲜周期临床妊娠率低,可考虑全部胚胎冷冻后移植。对于前次长长方案助孕失败的预期卵巢高反应患者,下一周期可考虑拮抗剂方案,亦可在改善基础状态并预防 OHSS 发生的基础上再次选择长长方案。

【关键词】 早卵泡期长效方案； 拮抗剂方案； 临床妊娠； 卵巢过度刺激综合征； 累积妊娠率； 妊娠所需时间

Comparison of early follicular phase prolonged protocol and gonadotropin-releasing hormone antagonist protocol in patients with expected high ovarian response:a retrospective cohort study and self-controlled study

Li Zhen, Zhang Junwei, Liu Hui, Guan Yichun, Li Jiaheng, Wang Xingling

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【Abstract】 **Objective** To investigate clinical outcomes and safety of the early follicular phase prolonged protocol and gonadotropin-releasing hormone antagonist (GnRH-A) protocol of patients with expected high ovarian response. **Methods** A retrospective cohort analysis of the expected high ovarian response patients during *in vitro* fertilization/intracytoplasmic sperm injection-embryo transfer (IVF/ICSI-ET) was performed in the Reproductive Center of the Third Affiliated Hospital of Zhengzhou University from September 2015 to May 2019,

including 1855 gonadotropin-releasing hormone agonist (GnRH-a) cycles and 720 GnRH-A cycles. The main outcome measures were the clinical outcomes, the incidence of moderate to severe ovarian hyperstimulation syndrome (OHSS), the pregnancy outcome of the first cycle of whole embryo freezing, cumulative pregnancy rate per oocytes retrieval cycle and time to pregnancy (TTP). And a self-controlled study was performed to compare the clinical outcomes of the patients who underwent early follicular phase prolonged protocol previously and underwent GnRH-A protocol or early follicular phase prolonged protocol later.

Results 1) There was no statistical difference between GnRH-a group and GnRH-A group in maternal age, body mass index (BMI), basal follicle-stimulating hormone (bFSH), anti-Müllerian hormone (AMH) and intima thickness on the human chorionic gonadotropin (hCG) trigger day ($P>0.05$). Compared with the Gn start-up [(170.12±53.94) IU], No. of obtained oocytes (20.60±9.92), No. of available embryos (10.96±6.59), and No. of high-quality embryos (6.47±4.97) in the GnRH-A group, the gonadotropins (Gn) start-up [(135.11±36.61) IU], No. of obtained oocytes (17.79±7.80), No. of available embryos (9.08±5.56), and No. of high-quality embryos (5.18±4.56) in the early follicular phase prolonged protocol group were significantly reduced correspondingly ($P<0.001$, $P<0.001$, $P<0.001$, $P=0.012$), while Gn used duration [(14.3±3.23) d], total Gn used dosage [(2 322.08±1 020.48) IU], incidence of moderate to severe OHSS after hCG trigger (9.54%) and fresh cycle clinical pregnancy rate (69.44%) increased significantly ($P<0.001$). 2) The clinical pregnancy rate and the abortion rate of the first cycle of whole embryo freezing were not statistically different between the two groups ($P>0.05$). 3) There was no statistically significant difference in the cumulative pregnancy rate between the two groups ($P>0.05$); the TTP of GnRH-A after fresh embryo transfer [(47.67±3.18) d] and frozen embryo cycle [(140.33±45.43) d] were significantly less than those in the early follicular phase prolonged protocol group [(81.25±3.72) d, (185.19±46.52) d, $P<0.001$]. But there was no significant difference in TTP between the two groups in the total transplantation period ($P>0.05$). 4) The comparison of early follicular phase prolonged protocol and GnRH-A protocol self-control showed that No. of available embryos (5.79±3.14) and No. of high-quality embryos (2.78±1.50) in early follicular phase prolonged protocol were significantly lower than those in GnRH-A group (10.14±4.74, 5.70±3.50) ($P=0.027$, $P=0.005$), and the total Gn used dosage [(2 535.80±1 212.17) IU] and moderate to severe OHSS incidence rate (4.55%) were significantly higher ($P=0.049$, $P=0.043$). 5) The comparison of early follicular phase prolonged protocol and self-control of early follicular phase prolonged protocol again showed that the BMI assisted by the early follicular phase prolonged protocol again [(24.63±2.99) kg/m²] was lower than that of the early follicular phase prolonged protocol in the first cycle [(25.01±3.12) kg/m², $P=0.049$], while the No. of high-quality embryos (4.00±3.58) and the clinical pregnancy rate of early follicular phase prolonged protocol again (52.10%) were significantly higher than those of the first cycle (2.56±2.12, 29.41%) ($P=0.046$, $P=0.004$). **Conclusion** For patients with high expected response, the GnRH-A protocol can significantly reduce the duration of Gn used, the dosage of Gn used

and the incidence of moderate to severe OHSS, increase the No. of oocytes, the No. of available embryos and the No. of high-quality embryos. The clinical pregnancy rate of the fresh cycle was lower in GnRH-A protocol, and whole embryo freezing can be considered. For the previous early follicular phase prolonged protocol patients, GnRH-A protocol can be considered next time, and the early follicular phase prolonged protocol can be selected again based on improvement of the basic state and prevention of OHSS.

【 Key words 】 Early follicular phase prolonged protocol; Gonadotropin-releasing hormone antagonist protocol; Clinical pregnancy; Ovarian hyperstimulation syndrome; Cumulative pregnancy rate; Time to pregnancy

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人绒毛膜促性腺激素注射日直径 ≥ 14 mm 卵泡数比例和卵泡输出率对 多囊卵巢综合征患者新鲜胚胎移植 妊娠率的影响

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【摘要】 目的 探讨多囊卵巢综合征(PCOS)患者控制性超促排卵中人绒毛膜促性腺激素(hCG)注射日直径 ≥ 14 mm 卵泡数比例和卵泡输出率(FORT)对卵泡期长效方案新鲜胚胎移植妊娠结局的影响。方法 回顾性队列研究分析 2017

年 5 月至 2018 年 5 月期间于郑州大学第三附属医院生殖医学中心行卵泡期长效方案新鲜胚胎移植 PCOS 患者的临床资料, 共计 811 个周期, 根据 hCG 注射日卵泡直径 ≥ 14 mm 数占比分为 3 组: A 组, 比例 $\leq 60\%$; B 组, 比例 $60\% \sim 80\%$; C 组, 比例 $\geq 80\%$ 。根据 FORT 分为 3 组: D 组, 比例 $\leq 40\%$; E 组, 比例 $40\% \sim 60\%$; F 组, 比例 $\geq 60\%$ 。比较各组患者的临床和实验室相关指标。按照移植结局, 将患者分为妊娠组及未妊娠组, 比较两组患者的临床资料, 并采用二元 logistic 回归分析影响临床妊娠的因素。结果 A、B、C 3 组获卵数依次增高 ($P < 0.001$); A 组的双原核 (2PN) 受精率 (59.78%) 低于 B 组 (62.40%, $P = 0.013$); 3 组胚胎种植率、临床妊娠率和活产率组间差异均无统计学意义 (P 均 > 0.05)。D、E、F 3 组获卵数依次增高 ($P < 0.001$), 但 F 组 2PN 受精率 (59.13%) 明显低于 D 组 (62.98%, $P = 0.009$) 和 E 组 (64.05%, $P < 0.001$); F 组胚胎种植率 (51.76%)、临床妊娠率 (62.72%)、活产率 (52.33%) 低于 E 组 (61.56%, $P = 0.002$; 72.70%, $P = 0.007$; 61.84%, $P = 0.011$), D 组 (56.77%、69.94%、59.54%) 与其他两组比较差异均无统计学意义 ($P > 0.05$)。妊娠组与未妊娠组相比, hCG 注射日直径 ≥ 14 mm 卵泡数占比差异无统计学意义 ($P > 0.05$), 而妊娠组 FORT 低于未妊娠组 ($P = 0.031$)。logistic 回归分析显示 FORT 是临床妊娠的独立影响因素 ($OR = 0.995$, 95% $CI = 0.974 \sim 1.016$, $P = 0.039$)。结论 在 PCOS 患者中, hCG 注射日直径 ≥ 14 mm 卵泡数占比不影响妊娠结局; FORT 对于预测妊娠结局具有重要意义, 中低比例 FORT 组可获得较好的妊娠结局。

【关键词】 卵泡径线; 卵泡输出率; 多囊卵巢综合征

Effect of the proportion of follicles with a diameter ≥ 14 mm on human chorionic gonadotropin injection day and follicular output rate on the pregnancy rate of fresh embryo transfer in patients with polycystic ovary syndrome

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【Abstract】 **Objective** To investigate the impact of the proportion of follicle diameter ≥ 14 mm on human chorionic hormone (hCG) injection day and follicular output rate (FORT) on the pregnancy outcome of fresh embryo transfer in patients with polycystic ovary syndrome (PCOS) by using long-acting gonadotropin-releasing hormone agonist (GnRH-a) long protocol in follicular phase. **Methods** The data of 811 fresh embryo transfer cycles of PCOS patients assisted by long-acting GnRH-a long protocol in follicular phase were analyzed retrospectively from May 2017 to May 2018 in the Center for Reproductive Medicine of the Third Affiliated Hospital of Zhengzhou University. According to the proportion of follicles with a diameter ≥ 14 mm on hCG injection day, patients were divided into three groups: group A (proportion $\leq 60\%$), group B (proportion $60\% \sim 80\%$) and group C (proportion $\geq 80\%$). According to the FORT, patients were divided into three groups: group D (proportion $\leq 40\%$), group E (proportion $40\% \sim 60\%$) and group F (proportion $\geq 60\%$). The clinical and laboratory indicators of patients in each group were compared and analyzed. According to the pregnancy

outcomes, patients were divided into pregnancy group and non-pregnancy group. The clinical data of the two groups were compared, and the influencing factors of clinical pregnancy outcomes were analyzed by binary logistic regression. **Results** The number of retrieved oocytes of groups A, B and C increased in turn ($P<0.001$). The fertility rate of two pronuclei (2PN) in group A (59.78%) was lower than that in group B (62.40%, $P=0.013$). There was no significant difference among the three groups in embryo implantation rate, clinical pregnancy rate and live birth rate ($P>0.05$). The number of retrieved oocytes in groups D, E and F increased ($P<0.001$), but the 2PN rate in group F (59.13%) was significantly lower than that in group D (62.98%, $P=0.009$) and group E (64.05%, $P<0.001$). Embryo implantation rate, clinical pregnancy rate and live birth rate in group F were lower than those in group E (51.76% vs. 61.56%, $P=0.002$; 62.72% vs. 72.70%, $P=0.007$; 52.33% vs. 61.84%, $P=0.011$), while those in group D (56.77%, 69.94%, 59.54%) were not significantly different from those in the other two groups ($P>0.05$). Compared with pregnancy group, the proportion of dominant follicles on hCG injection day in non-pregnancy group was not significantly different ($P>0.05$), while FORT in pregnancy group was lower than that in non-pregnancy group ($P=0.031$). Logistic regression analysis showed that FORT was an independent influencing factor for clinical pregnancy [$OR=0.995$, 95% $CI=0.974-1.016$, $P=0.039$]. **Conclusion** In PCOS patients, the proportion of follicles with a diameter ≥ 14 mm on hCG injection day does not affect pregnancy outcomes, the FORT is of great significance in predicting pregnancy outcomes, and the middle and low proportion of FORT group can obtain better pregnancy outcomes.

【Key words】 Follicle diameter; Follicular output rate; Polycystic ovary syndrome

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·临床研究·

人绒毛膜促性腺激素注射日孕酮/ 成熟卵子数比值对高龄患者新鲜胚 胎移植后活产率的预测价值

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【摘要】 目的 探究体外受精-胚胎移植 (IVF-ET) 周期人绒毛膜促性腺激素 (hCG) 注射日孕酮/成熟卵子数比值 (PMOI) 对高龄患者新鲜胚胎移植后活产率的预测价值。方法 回顾性分析 2015 年 1 月 1 日至 2018 年 6 月 30 日期间在中国人民解放军联勤保障部队第 901 医院生殖医学中心行 IVF-ET 助孕高龄患者的临床资料, 共 277 个移植周期。按 hCG 注射日 PMOI 水平分为 $\leq 0.075 \mu\text{g/L}$ 组 (A 组)、 $0.075 \sim 0.190 \mu\text{g/L}$ 组 (B 组) 及 $\geq 0.190 \mu\text{g/L}$ 组 (C 组), 比较 3 组患者临床资料和妊娠结局, 并采用单因素和多因素 logistic 回归分析及受试者工作特征 (ROC) 曲线探讨 hCG 注射日 PMOI 对高龄患者活产率的预测价值。结果 C 组患者的卵泡刺激素 (FSH) 水平 [(10.27 \pm 3.24) IU/L] 显著高于 A 组 [(8.20 \pm 1.93) IU/L, $P < 0.001$] 和 B 组 [(8.87 \pm 2.54) IU/L, $P = 0.002$] 抗苗勒管激素 (AMH) [(1.97 \pm 1.27) $\mu\text{g/L}$] 及窦卵泡计数 (AFC) (6.22 \pm 4.08) 显著低于 A 组 [(3.37 \pm 1.94) $\mu\text{g/L}$, $P < 0.001$; 12.19 \pm 6.29, $P < 0.001$] 和 B 组 [(2.46 \pm 1.63) $\mu\text{g/L}$, $P = 0.029$; 9.74 \pm 4.83, $P < 0.001$], 晚期流产率 (25.00%) 显著高于 A 组 (0%, $P = 0.020$), 活产率 (8.70%) 显著低于 A 组 (24.29%, $P = 0.013$)。logistic 回归分析显示患者年龄 ($OR = 0.750$, $P = 0.029$) 和 hCG 注射日 PMOI ($OR = 0.006$, $P = 0.044$) 是影响活产率的危险因素。ROC 曲线显示, hCG 注射日 PMOI 对高龄患者活产率有预测价值, 敏感度为 43.5%, 特异度为 80.0%, 截断值为 0.144 $\mu\text{g/L}$ 。结论 高水平的 hCG 注射日 PMOI 是影响高龄患者新鲜周期活产率的危险因素, 对高龄患者助孕结局有一定的预测价值。

【关键词】 人绒毛膜促性腺激素; 受精, 体外; 胚胎移植; 活产率; 高龄; 孕酮/成熟卵子数比值; 截断值

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Predictive value of progesterone to number of mature oocytes index for live birth rate on human chorionic gonadotropin injection day after fresh embryo transfer in advanced age women

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【Abstract】 **Objective** To explore the predictive value of progesterone to number of mature oocytes index (PMOI) for live birth rate on human chorionic

gonadotropin (hCG) injection day after fresh embryo transfer of advanced age women during *in vitro* fertilization-embryo transfer (IVF-ET) cycles. **Methods** The clinical data of 277 IVF-ET cycles with advanced age women in Reproductive Medicine Center, the 901th Hospital of the Joint Logistic Support Force of People's Liberation Army from January 1, 2015 to June 30, 2018 were analyzed retrospectively. According to the hCG injection day PMOI level, the patients were divided into three groups: group A ($\leq 0.075 \mu\text{g/L}$), group B ($0.075\text{--}0.190 \mu\text{g/L}$) and group C ($\geq 0.190 \mu\text{g/L}$). The clinical data and pregnancy outcomes of the three groups were compared. Afterwards, univariate and multivariate logistic regression and receiver operating characteristic (ROC) curve were applied to explore the predictive value of PMOI on hCG injection day for live birth rate of advanced age women. **Results** The follicular-stimulating hormone (FSH) level [(10.27 ± 3.24) IU/L] in group C was significantly higher, the anti-Müllerian hormone (AMH)[$(1.97\pm 1.27) \mu\text{g/L}$] and antral follicle count (AFC) (6.22 ± 4.08) were significantly lower than those in group A [(8.20 ± 1.93) IU/L; $(3.37\pm 1.94) \mu\text{g/L}$; 12.19 ± 6.29 , $P<0.001$] and group B [(8.87 ± 2.54) IU/L, $P=0.002$; $(2.46\pm 1.63) \mu\text{g/L}$, $P=0.029$; 9.74 ± 4.83 , $P<0.001$], the late abortion rate (25.00%) was significantly higher than that in group A (0%, $P=0.020$), the live birth rate (8.70%) was significantly lower than that in group A (24.29%, $P=0.013$). The logistic regression model demonstrated that age ($OR=0.750$, $P=0.029$) and hCG injection day PMOI ($OR=0.006$, $P=0.044$) were risk factors to live birth rate. The ROC curve showed that hCG injection day PMOI may be a promising candidate for prediction of live birth rate of advanced age women, and the sensitivity and specificity were 43.5% and 80.0% respectively, the cut-off value was $0.144 \mu\text{g/L}$. **Conclusion** Elevated hCG injection day PMOI level may be a risk factor for live birth rate and a promising candidate for prediction of pregnancy outcome of advanced age women in fresh IVF-ET cycles.

【Key words】 Human chorionic gonadotropin; Fertilization *in vitro*; Embryo transfer; Live birth rate; Advanced age; Progesterone to number of mature oocytes index; Cut-off value

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女性血清维生素 D 水平与早期自然流产的相关性研究

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【摘要】 目的 探讨女性血清维生素 D 水平与早期自然流产的关系,并探索维生素 D 的作用机制。方法 本研究采用病例对照研究,选择 2018 年 3 月至 2019 年 12 月期间在桐庐县第一人民医院就诊的 52 例自然流产女性为研究组,因非意愿妊娠要求终止早期妊娠的患者 50 例作为对照组,育龄期非妊娠状态的女性体检者 40 例作为正常组,比较三组患者血清中维生素 D₃、钙离子及甲状旁腺激素(PTH)的浓度,收集研究组和对照组人工流产后的绒毛组织及蜕膜组织,采用 RT-PCR 检测维生素 D 受体(VDR)及 1 α -羟酶(CYP27B1 基因编码)的 mRNA 表达量,以免疫组织化学法定位并检测两者的蛋白相对表达量。结果 研究组血清中维生素 D₃浓度 [12.4(10.1,17.2) μ g/L]均低于对照组 [16.7(13.5,21.9) μ g/L, $P<0.0001$]和正常组 [18.9(15.6,26.4) μ g/L, $P=0.0056$],而血清中钙离子和 PTH 浓度组间差异均无统计学意义($P>0.05$)。在蜕膜组织中,研究组的 VDR mRNA [0.8713(0.6686,1.0857)]及蛋白表达量 [3.0(2.5,4.0)]较对照组的 mRNA [1.1027(0.8977,1.3571)]及蛋白表达量 [4.5(3.5,5.5)]降低,且差异有统计学意义($P=0.0003$; $P<0.0001$),而 CYP27B1 mRNA 及蛋白表达量与对照组相比有下降趋势,但差异无统计学意义($P>0.05$)。在绒毛组织中,研究组和对照组相比,无论是 VDR 还是 CYP27B1 的 mRNA 及蛋白表达量差异均无统计学意义($P>0.05$)。结论 女性早期自然流产可能与低血清维生素 D 水平有关,低浓度维生素 D 主要通过下调蜕膜组织中的 VDR 表达导致早期自然流产的发生。

【关键词】 维生素 D; 蜕膜; 绒毛膜; 早期妊娠; 自然流产
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Study on the relationship between serum vitamin D level and early spontaneous abortion

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【Abstract】 Objective To investigate the relationship between serum vitamin D levels and early spontaneous abortion and to elucidate the mechanism of

vitamin D in pregnancy. **Methods** A total of 142 women at the Tonglu First People's Hospital in Zhejiang Province from March 2018 to December 2019 were enrolled in this case-control study. All the participants were divided into three groups and determined as experimental group (52 early spontaneous abortion women), control group (50 women who terminated an early pregnancy due to unintended pregnancy) and normal group (40 non-pregnancy women of childbearing age). The concentrations of serum vitamin D₃, calcium ion (Ca²⁺) and parathyroid hormone (PTH) were observed in the three groups. The chorionic villus and decidual tissues of experimental and control groups were firstly collected. Using RT-PCR, we identified the mRNA levels of vitamin D-related substances, the vitamin D receptor (VDR) and 1 α -hydroxylase (encoded by *CYP27B1* gene). Furthermore, immunohistochemical method was used to detect the VDR and *CYP27B1* expressions at protein level in two groups. **Results** The serum vitamin D concentration in experimental group [12.4(10.1,17.2) μ g/L] was significantly lower than that of control group [16.7(13.5,21.9) μ g/L, $P<0.000\ 1$] and normal group [18.9(15.6,26.4) μ g/L, $P=0.005\ 6$], whereas the concentrations of Ca²⁺ and PTH showed no significant difference ($P>0.05$). In the decidual tissues, expression levels of *VDR* mRNA [0.871 3(0.668 6,1.085 7)] and protein [3.0(2.5,4.0)] were decreased in experimental group compared with those in control group [1.102 7(0.897 7,1.357 1), 4.5(3.5,5.5)], and the difference was statistically significant (mRNA $P=0.000\ 3$; protein $P<0.000\ 1$). *CYP27B1* showed no significant difference, despite the reduction compared with control group ($P>0.05$). In the chorionic villus, compared with control group, the differences in mRNA and protein expression levels of both *VDR* and *CYP27B1* were not statistically significant in experimental group ($P>0.05$). **Conclusion** Early spontaneous abortion in women might be associated with low serum vitamin D levels. Importantly, vitamin D deficiency in pregnancy could contribute to the downregulation of VDR expression in decidual tissues, which leads to the early spontaneous abortion.

【Key words】 Vitamin D; Decidua; Chorion; Early pregnancy; Spontaneous abortion

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· 实验研究 ·

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自制冷冻片微型载体 (Strawtop)

微量精液冻存效果的实验研究

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王荣祥和喻乔对本文有同等贡献

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【摘要】 目的 对自制冷冻片微型载体 (Strawtop) 法与麦管法冷冻保存人微量精液的冻存效果进行系统评价。方法 采用前瞻性研究分析 2018 年 5 月 1 日至 2018 年 6 月 30 日期间于同济大学附属东方医院生殖医学中心行卵胞质内单精子显微注射 (ICSI) 助孕治疗的患者捐献的部分精液样本, 比较自制 Strawtop 法与麦管法冷冻人精子复苏后的冷冻复苏率、DNA 碎片指数 (DNA fragmentation index, DFI)、超显微结构和受精能力与胚胎发育情况。结果 Strawtop 法冻存人精子的冷冻复苏率 ($46.8\% \pm 17.1\%$) 显著高于麦管法 ($23.1\% \pm 13.7\%$, $P=0.001$) ; 与冷冻前 ($18.9\% \pm 11.6\%$) 相比, 麦管法 ($33.5\% \pm 15.0\%$) 冷冻精子复苏后的 DFI 显著增加 ($P=0.019$) , 而 Strawtop 法冻融人精子的 DFI ($23.4\% \pm 11.7\%$) 与冷冻前相比差异无统计学意义 ($P=0.375$) ; Strawtop 法对冷冻精子超显微结构的损伤低于麦管法; Strawtop 法冻融精子、麦管法冻融精子和新鲜精子的正常受精率、卵裂率和受精后 48 h (第 2 日) 的优质胚胎率差异均无统计学意义 ($P>0.05$) 。结论 Strawtop 法冷冻人微量精液冷冻复苏率高于麦管法, 复苏精子的损伤较小, 且复苏后无需离心洗涤即可直接用于 ICSI, 具有较高的临床应用价值。

【关键词】 无精子症; 严重少精子症; 微量精液冷冻; 麦管法; Strawtop 法

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Experimental study on low volume sperm cryopreservation using Strawtop micro-carrier

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【 Abstract 】 **Objective** To evaluate the cryopreservation effect of the home-made Strawtop micro-carrier method and Straw method for cryopreservation of human low volume sperm. **Methods** A prospective study was performed to analyze the post-thaw results of cryopreserved human sperm using the home-made Strawtop method and Straw method. Compare the survival rate, sperm DNA fragmentation index (DFI), ultrastructure, fertilization ability and embryo developmental competence of donated semen samples from the patients who underwent intracytoplasmic sperm injection (ICSI) treatment in Center for Reproductive Medicine, Shanghai East Hospital, Tongji University School of Medicine during the period from May 1, 2018 to June 30, 2018. **Results** The survival rate of Strawtop group ($46.8\% \pm 17.1\%$) was significantly higher than that of Straw group ($23.1\% \pm 13.7\%$, $P=0.001$). Compared with fresh sperm ($18.9\% \pm 11.6\%$), Straw method ($33.5\% \pm 15.0\%$) significantly increased the sperm DFI ($P=0.019$), while Strawtop method didn't ($23.4\% \pm 11.7\%$, $P=0.375$). The sperm ultrastructure of Strawtop group was superior to that of Straw group. There was no difference among Strawtop, Straw and fresh group in normal fertilization rates, cleavage rates and day 2 high-quality embryo rates. **Conclusion** For human low volume sperm cryopreservation, the Strawtop method was simple and convenient. The survival rate of Strawtop method was higher than that of straw method and the sperm could be used for ICSI directly after thawing. The strawtop method is worth to be widely used in clinical practice.

【 Key words 】 Azoospermia; Severe oligospermia; Low volume sperm cryopreservation; Straw method; Strawtop method

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· 现场调查 ·

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结构方程模型下体外受精助孕患者自我效能量表的信效度研究

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【摘要】 目的 探讨合理用药自我效能量表 (Self-efficacy for Appropriate Medication Use Scale , SEAMS) 在体外受精-胚胎移植 (*in vitro* fertilization-embryo transfer , IVF-ET) 助孕患者中的适用性。方法 应用 SEAMS 对 494 名上海市交通大学医学院附属瑞金医院生殖医学中心就诊的 IVF 助孕患者进行调查 , 采用 SPSS 和 AMOS 软件进行模型的构建 , 评定该量表的信效度。结果 SEAMS 总量表的 Cronbach's α 是 0.938 , 3 个维度的 Cronbach's α 在 0.800~0.909 之间 ; 总量表的折半信度是 0.888 , 3 个维度的折半信度在 0.800~0.890 之间 ; 总量表的重测信度是 0.884 , 3 个维度的重测信度在 0.731~0.824 之间。SEAMS 得分与 Morisky 服药依从性问卷得分的相关系数为 0.789 ($P<0.001$) 。量表进行探索性主因子进一步分析 , 结果显示有 3 个公因子 , 累积贡献率是 72.99% ($KMO=0.929$) ; 经验证性因子分析进一步验证 , 得到 3 因子的结构方程模型 : $\chi^2=121.891$, $\chi^2/df=2.102$, 近似均方根残差 (RMSEA) =0.067 , 比较拟合指数 (GFI) =0.929 , 规范拟合指数 (NFI) =0.947 , 增量拟合指数 (IFI) =0.971 , 比较拟合指数 (CFI) =0.971 , 各变量的因子载荷在 0.70~0.88 ($P<0.001$) , 模型拟合良好。结论 SEAMS 量表有良好的信效度 , 可以用来评价 IVF 助孕患者的用药依从性。

【关键词】 受精 , 体外 ; 胚胎移植 ; 合理用药自我效能量表 ; 信度 ; 效度 ; 结构方程模型 ; 验证性因子分析

Reliability and validity of Self-efficacy for Appropriate Medication Use Scale in the *in vitro* fertilization patients medication adherence based on structural equation model

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【Abstract】 Objective To explore the applicability of Chinese version Self-efficacy for Appropriate Medication Use Scale (SEAMS) in evaluating the medication adherence of patients with *in vitro* fertilization (IVF). **Methods** A total of 494 patients with IVF were selected from Ruijin Hospital of Shanghai Jiao Tong University School of Medicine using simple random sampling method. Using SPSS and AMOS software to build of the model and the reliability and validity of SEAMS were evaluated in the study. **Results** SEAMS had a good reliability, with the Cronbach's α of 0.938. The Cronbach's α of the three branch scales was 0.800–0.909. The split-half reliability of SEAMS was 0.888, which the split-half reliabilities of the three branch scales were 0.800–0.890. The test-retest reliability of SEAMS was 0.884. The test-retest reliabilities of the three branch scales were 0.731–0.824. Using Morisky questionnaire as an external criterion, the correlation coefficient of SEAMS and Morisky scores was 0.789 ($P<0.001$). The factor analysis showed that there were three main factors with a cumulative variance rate of 72.99% (KMO=0.929). The confirmatory factor analysis revealed a good fit of three factors. The results showed that $\chi^2=121.891$, $\chi^2/df=2.102$, root mean square error of approximation (RMSEA)=0.067, goodness of fit index (GFI)=0.929, normal fit index (NFI)=0.947, incremental fit index (IFI)=0.971, comparative fit index (CFI)=0.971. Each factor had a load capacity of 0.70–0.88 ($P<0.001$), and the model fitting was good. **Conclusion** SEAMS has a good reliability and validity, and can be used to evaluate the medication adherence of patients with IVF in our country.

【Key words】 Fertilization *in vitro*; Embryo transfer; Self-efficacy for Appropriate Medication Use Scale; Reliability; Validity; Structural equation model; The confirmatory factor analysis

· 个案报道 ·

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卵巢过度刺激综合征并发颅内血栓 1 例病案报道

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【摘要】 目的 探讨卵巢过度刺激综合征 (ovarian hyperstimulation syndrome , OHSS) 并发血栓的高危因素、预防、治疗及预后。方法 对青岛大学附属医院生殖医学科 1 例行控制性超促排卵(controlled ovarian hyperstimulation , COH) 诱发重度 OHSS 并发颅内血栓的患者的治疗过程进行分析报道。结果 患者经颅内取栓、抗凝、合并症处理后顺利康复，再经 2 次冻融胚胎移植顺利分娩 1 名健康男婴。结论 重度 OHSS 并发血栓形成是 COH 过程中罕见却极其严重的并发症，甄别 OHSS 的高危因素、妥当处理合并症、个体化用药预防 OHSS 发生的最佳方案。

【关键词】 卵巢过度刺激综合征； 颅内血栓； 高危因素； 预防； 治疗

One case report of intracranial thrombosis after ovarian hyperstimulation syndrome

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【 Abstract 】 Objective To discuss the high risk factors, preventions, treatments and prognosis of thrombosis after ovarian hyperstimulation syndrome (OHSS). **Methods** The data of one case of severe OHSS complicated with intracranial thrombus induced by controlled ovarian hyperstimulation (COH) in Department of Reproductive Medicine, the Affiliated Hospital of Qingdao University were analyzed. **Results** After the treatment of intracranial thrombectomy, anticoagulation and complications, the patient recovered successfully, and then gave birth to a healthy baby boy after twice frozen-thawed embryo transplantation. **Conclusion** Severe OHSS complicated with thrombosis is a rare but extremely serious complication in the course of COH. It is the best way to prevent OHSS to identify the high risk factors, properly handle the complications and individualized medication.

【 Key words 】 Ovarian hyperstimulation syndrome; Intracranial sinus thrombosis; High risk factors; Prevention; Treatment

·综述·

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抗苗勒管激素用于多囊卵巢综合征诊断的研究进展

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【摘要】 多囊卵巢综合征 (polycystic ovary syndrome, PCOS) 患者血清中抗苗勒管激素 (anti-Müllerian hormone, AMH) 水平较正常女性高。近年越来越多的研究提示, AMH 与雄激素相互作用导致 PCOS 患者卵泡发育障碍, AMH 可作为诊断 PCOS 的生化指标, 尤其是在高雄激素血症的 PCOS 患者中。本文就 AMH 用于 PCOS 诊断的前景及挑战进行综述。

【关键词】 多囊卵巢综合征; 抗苗勒管激素; 高雄激素血症

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Research progress of anti-Müllerian hormone in the diagnosis of polycystic ovary syndrome

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【Abstract】 The level of anti-Müllerian hormone (AMH) in the serum of patients with polycystic ovary syndrome (PCOS) was higher than that of normal women. In recent years, more and more studies have suggested that the interaction between AMH and androgen causes follicular developmental disorder in PCOS patients, and AMH can be used as a biochemical indicator for the diagnosis of PCOS, especially in PCOS patients with hyperandrogenism. This paper reviews the prospects and challenges of AMH in the diagnosis of PCOS.

【Key words】 Polycystic ovary syndrome; Anti-Müllerian hormone; Hyperandrogenism

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• 综 述 •

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多囊卵巢综合征患者雄激素与代谢表型关系研究进展

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【摘要】 多囊卵巢综合征 (polycystic ovary syndrome, PCOS) 是育龄期女性常见生殖内分泌疾病, 不仅影响生殖, 还与代谢紧密联系。雄激素过多是 PCOS 重要特征, 糖脂代谢异常是 PCOS 患者常见的代谢紊乱。PCOS 的雄激素过多和胰岛素抵抗相互关联, 两者又与脂代谢异常有关。三者之间的紧密联系影响 PCOS 的发生发展过程。临床上对 PCOS 患者代谢异常的早期发现和有效治疗对 PCOS 患者远期并发症的预防具有重要意义。本文将从 PCOS 中的雄激素过多、PCOS 代谢异常原因及两者间潜在联系和治疗等方面做一综述。

【关键词】 雄激素; 多囊卵巢综合征; 胰岛素抵抗; 脂代谢

Research progress in relationship between androgen and metabolic phenotype in patients with polycystic ovary syndrome

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【Abstract】 Polycystic ovary syndrome (PCOS) is a common reproductive endocrine disease in women of reproductive age, which not only affects reproduction, but also has a close relationship with metabolism. Androgen excess is an important characteristic, and abnormal glucose and lipid metabolism are

common metabolic disorders in PCOS women. Androgen excess is correlated with insulin resistance in PCOS, which is also associated with dyslipidemia. The close link among the three factors promotes the occurrence and development of PCOS. Early screen and control of metabolic abnormalities would be beneficial for the complication prevention for PCOS patients for long term. In this paper, we discussed androgen excess, metabolic abnormalities and their relationship, as well as treatment in PCOS.

【Key words】 Androgen; Polycystic ovary syndrome; Insulin resistance; Lipid metabolism

· 综述 ·

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梗阻性无精子症的遗传学研究进展

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【摘要】 无精子症占男性不育的 10%~15%, 约占男性总体人群的 1%, 其中梗阻性无精子症占 40%。梗阻性无精子症可以由多种因素导致, 其中包括男性生殖道炎症及遗传学因素等, 但是由于梗阻性无精子症患者睾丸内精子发生并无明显异常, 睾丸穿刺取精结合辅助生育技术即可使患者生育自身子代, 因此其遗传学病因常常被忽略, 继而后期的辅助生殖策略以及子代出生缺陷研究也常常被忽视。本文就梗阻性无精子症的人群遗传学病因以及梗阻性无精子症动物模型两方面问题的研究进展进行综述, 以期对临床诊疗、遗传咨询以及男性避孕药物研发提供新思路。

【关键词】 男性不育; 梗阻性无精子症; 遗传学

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Advances in the genetics of obstructive azoospermia

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【Abstract】 Azoospermia accounts for 10%–15% of male infertility, with the prevalence of 1% in male population. Obstructive azoospermia (OA) accounts for 40% of azoospermia and can be caused by a variety of factors, including male reproductive duct inflammation and genetic factors. Given the fact that the spermatogenesis is normal in the testis of OA patients, the OA patients can have their own offspring through testicular biopsy and sperm retrieval followed by assisted reproductive technology (ART). Therefore, the genetic etiology of OA is often overlooked. Subsequently, studies of the following ART strategies and offspring birth defects are also ignored. This article reviewed the genetic disorders of OA patients, and the animal model with OA, providing new ideas for management of OA patients, genetic counseling, and development of male contraceptives.

【Key words】 Male infertility; Obstructive azoospermia; Genetics

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·综述·

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分泌蛋白组学在生殖领域中的研究进展

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【摘要】 “分泌蛋白”是指由活细胞所分泌的丰富的、具有复杂生理功能的一系列蛋白，包括细胞因子、趋化因子、激素、消化酶、抗体、胞外蛋白酶和毒素等，这些蛋白参与细胞信号转导、粘连、迁移和免疫防御等多种生物过程，发挥重要的生理作用。近年来，蛋白组学技术飞速发展，极大地促进了分泌蛋白组学的研究和发展。分泌蛋白组学已经被广泛应用于人类生殖领域的探索，并鉴定了许多蛋白质，这些蛋白质可能是人类辅助生殖技术成功妊娠的潜在生物标志物或治疗目标。本文综述了分泌蛋白组学在人卵泡液、胚胎发育及子宫内膜分泌物中的研究进展，为分泌蛋白组学在人类生殖领域研究中的深入应用提供借鉴。

【关键词】 生殖技术，辅助；分泌蛋白组学；卵泡液；胚胎发育；子宫内膜分泌物

Research progress of secretomics in the field of reproduction

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【Abstract】 "Secreted protein" refers to a series of proteins with complex physiological functions secreted by living cells, including cytokines, chemokines, hormones, digestive enzymes, antibodies, extracellular proteases and toxins. These proteins play important physiological roles in a variety of biological processes, such as cell signal transduction, adhesion, migration and immune defense. In recent years, the rapid development of proteomics technology has greatly promoted the research of secretomics. Secretomics has been widely used in the field of human reproduction, and many proteins have been identified, which may be potential biomarkers or therapeutic targets for successful pregnancy in human assisted reproductive techniques. In this paper, the research progress of secretomics in human follicular fluid, embryonic development and endometrial secretions were reviewed in order to provide reference for the further application of secretomics in the field of human reproduction.

【Key words】 Reproductive techniques, assisted; Secretomics; Follicular fluid; Embryonic development; Endometrial secretions

·综述·

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肠道菌群与生殖系统疾病的相关性研究进展

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【摘要】 肠道菌群作为人体微生态环境的一个部分,对维持身体健康、保障人体正常生命活动起着重要作用。越来越多的研究表明,肠道菌群参与了多种生殖系统相关疾病的发生发展以及转归。肠道微生态的紊乱与多囊卵巢综合征、子宫内膜异位症、阴道内环境以及男性生殖系统疾病相关,因此,调节肠道菌群对生殖相关疾病的治疗有积极意义。该文就目前肠道菌群与生殖相关疾病之间的相关性研究进行综述。

【关键词】 肠道菌群; 多囊卵巢综合征; 子宫内膜异位症; 阴道内环境; 精液

Research progress on the relationship between intestinal flora and reproductive system diseases

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【Abstract】 As a part of human microecological environment, intestinal flora plays an important role in maintaining health and ensuring normal life activities of human body. More and more studies have shown that intestinal flora is involved in the occurrence, development and prognosis of a variety of reproductive system-related diseases. It has been confirmed that intestinal microecological disorders are associated with polycystic ovary syndrome, endometriosis, vaginal environment and male reproductive system diseases. The adjustment of intestinal flora is not only of positive significance in the treatment of reproductive-related diseases, but also can affect the offspring. This paper reviews the current studies on the relationship between intestinal flora and reproduction-related diseases.

【Key words】 Intestinal flora; Polycystic ovary syndrome; Endometriosis; Vaginal environment; Semen