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编 辑

中华生殖与避孕杂志
编辑委员会
200237,上海市老沪闵路779号
电话:(021)64438169
传真:(021)64438975
Email:rande@sippr.org.cn
http://zhshzybyzz.yiigle.com

总编辑

乔 杰

编辑部主任

王 健

出 版

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Editing

Editorial Board of Chinese Journal of
Reproduction and Contraception
779 Laohumin Road, Shanghai 200237, China
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Fax: 0086-21-64438975
Email: randc@sippr.org.cn
http://zhshzybyzz.yiigle.com

Editor-in-Chief

Qiao Jie

Managing Director

Wang Jian

Publishing

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Fax: 0086-21-64438975
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无精子症诊疗中国专家共识

中国医师协会生殖医学专业委员会生殖男科学组无精子症诊疗中国专家共识编写组

通信作者: 熊承良, Email: clxiong951@sina.com, 电话: +86-27-

82742288; 李铮, Email: 13564783816@163.com, 电话: +86-

13564783816; 洪锴, Email: kenhong99@hotmail.com, 电话:

+86-13501213023

【摘要】 无精子症是男性不育症中最严重的一种情况。为进一步规范无精子症的诊疗过程,由中国医师协会生殖医学专业委员会生殖男科学组发起,组织无精子症领域的专家成立编写小组,基于临床实践和已发表文献共同讨论和制定此共识。共识涉及梗阻性无精子症、非梗阻性无精子症的诊断与治疗策略,以及无精子症的遗传学咨询、与其他病因相关联的无精子症、辅助生殖技术、生育力保存和健康管理等方面内容,旨在为从事生殖医学、男科学专业医务人员提供专家咨询建议和诊疗参考。

【关键词】 无精子症; 梗阻性无精子症; 非梗阻性无精子症; 生殖技术, 辅助; 专家共识

Chinese experts' consensus on the diagnosis and treatment of azoospermia

Chinese Expert Consensus Compilation Group for Azoospermia Diagnosis and Treatment, Reproductive Andrology Group, Reproductive Medicine Professional Committee of Chinese Medical Doctor Association

Corresponding authors: Xiong Chengliang, Email: clxiong951@sina.com, Tel: +86-27-82742288; Li Zheng, Email: 13564783816@163.com, Tel: +86-13564783816; Hong Kai, Email: kenhong99@hotmail.com, Tel: +86-13501213023

【Abstract】 Azoospermia is one of the most serious conditions of male infertility. In order to further standardize the diagnosis and treatment of azoospermia in China, the Reproductive Andrology Group of the Reproductive Medicine Professional Committee of Chinese Medical Doctor Association grouped

experts from the field of azoospermia to come together and develop an expert consensus based on the published literature. The consensus covers such aspects of diagnosis and treatment strategies of obstructive azoospermia, non-obstructive azoospermia, as well as genetic counseling, azoospermia associated with other causes, assisted reproductive technology, fertility preservation and health management for azoospermia. The present consensus aims to provide expert consultations and advices for medical professionals engaged in reproductive medicine and andrology.

【Key words】 Azoospermia; Obstructive azoospermia; Non-obstructive azoospermia; Reproductive technology, assisted; Expert consensus

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少精子症诊疗中国专家共识

中国医师协会生殖医学专业委员会生殖男科学组少精子症诊疗中国专家共识编写组

通信作者: 熊承良, Email: clxiong951@sina.com, 电话: +86-27-

82742288; 谷翊群, Email: ygu90@hotmail.com, 电话: +86-10-

62148629; 康跃凡, Email: fjkylf@163.com, 电话: +86-591-

87556044

【摘要】 少精子症作为男性不育最常见的类型之一,是指射出体外的精液中精子总数(或精子浓度)低于正常生育力男性精液检查参考值下限。本共识由中国医师协会生殖医学专委会生殖男科学组组织专家编写,从少精子症的病因、诊断流程以及个体化治疗方案等多个方面进行了深入的探讨,提出基于2次及以上精液检测结果的分级标准;推荐进行生殖内分泌激素检查、影像学检查、遗传学检测(疑似遗传因素)等明确少精子症的病因;推荐针对少精子症病因的治疗(激素治疗、精索静脉曲张结扎术、精道内镜手术等)、抗氧化治疗、中西医结合治疗等,以及辅助生殖技术助孕(经上述常规治疗手段无效时,合理选择宫腔内人工授精、体外

受精、卵胞质内单精子显微注射、植入前遗传学检测等方案)。本共识可为从事生殖医学、男科学的专业医务人员提供专家咨询和建议。

【关键词】 少精子症； 诊断； 治疗； 辅助生殖； 专家共识

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Chinese experts' consensus on the diagnosis and treatment of oligozoospermia

Chinese Expert Consensus Compilation Group for Oligozoospermia Diagnosis and Treatment, Reproductive Andrology Group, Reproductive Medicine Professional Committee of Chinese Medical Doctor Association

Corresponding authors: Xiong Chengliang, Email: clxiong951@sina.com, Tel: +86-27-82742288; Gu Yiqun, Email: ygu90@hotmail.com, Tel: +86-10-62148629; Kang Yuefan, Email: fjkyf@163.com, Tel: +86-591-87556044

【 Abstract 】 As one of the most common types of male infertility, oligozoospermia is defined as that the total number of sperm (or sperm concentration) in the ejaculated semen is lower than the lower limit of the reference value of normal fertility male semen examination. This consensus was drafted by experts organized by Reproductive Andrology Group, Reproductive Medicine Professional Committee of Chinese Medical Doctor Association, and conducted in-depth discussions on the epidemiology, etiology, diagnosis process, and individualized management of oligozoospermia. It was proposed that oligozoospermia was graded based on the twice or more results of semen analysis. And reproductive endocrine hormone examination, imaging examination, genetic testing (suspected genetic factors), etc. are recommended to determine the cause of oligozoospermia. Furthermore, we recommend treatments according to the causes of oligozoospermia (hormonal therapy, varicocelelectomy, endoscopic surgery of the seminal tract, etc.), antioxidant therapy, integrated Traditional Chinese and Western Medicine, etc. Additionally, when the above-mentioned conventional treatments are invalid, assisted reproduction, including intrauterine insemination, *in vitro* fertilization, intracytoplasmic sperm injection, preimplantation genetic testing, was recommended reasonably. This consensus can provide expert consultation and advice for medical professionals engaged in reproductive medicine and andrology.

【 Key words 】 Oligozoospermia; Diagnosis; Treatment; Assisted reproduction; Expert consensus

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弱精子症诊疗中国专家共识

中国医师协会生殖医学专业委员会生殖男科学组弱精子症诊疗中国专家共识编写组

通信作者: 熊承良, Email: clxiong951@sina.com, 电话: +86-27-

82742288; 谷翊群, Email: yqgu90@126.com, 电话: +86-10-

62148629; 唐运革, Email: tyg813@126.com, 电话: +86-20-

87696536

【摘要】 弱精子症是男性不育最常见的类型之一,是复杂多因素作用的结果,有 30%~40%的病例无法明确病因和发病机制。有鉴于此,中国医师协会生殖医学专业委员会生殖男科学组组织了生殖男科领域的专家,从弱精子症的病因、诊断流程以及个体化治疗方案等多个方面进行了深入的探讨。主要包括基于 2 次及以上精液检测结果的弱精子症分级标准;建议进行精子存活率检测、形态学分析、阴囊超声检查、经直肠超声检查和遗传学检测等明确弱精子症的病因;推荐针对弱精子症病因的治疗,经验性治疗以及辅助生殖技术助孕。本共识可为从事生殖医学、男科学的专业医务人员提供专家咨询建议和诊疗参考方案。

【关键词】 弱精子症; 诊断; 治疗; 专家共识

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Chinese experts' consensus on the diagnosis and treatment of asthenozoospermia

Chinese Expert Consensus Compilation Group for Asthenozoospermia Diagnosis and Treatment, Reproductive Andrology Group, Reproductive Medicine Professional Committee of Chinese Medical Doctor Association

Corresponding authors: Xiong Chengliang, Email: clxiong951@sina.com, Tel: +86-27-82742288; Gu Yiqun, Email: yqgu90@126.com, Tel: +86-10-62148629; Tang Yunge, Email: tyg813@126.com, Tel: +86-20-87696536

【Abstract】 Asthenozoospermia is one of the most common types of male infertility. As a result of complex and multi-factorial effects, about 30% to 40% of the cases cannot be clarified with clear causes and pathogenesis. Therefore, Reproductive Andrology Group, Reproductive Medicine Professional Committee of Chinese Medical Doctor Association organized experts in the field of reproductive

andrology to conduct in-depth discussions on the causes of asthenozoospermia, diagnosis procedures, and individualized managements. The main points include grading of asthenozoospermia based on the twice or more results of semen analysis; recommending sperm vitality and morphological analysis, scrotal ultrasound examination, transrectal ultrasonography, genetic testing, etc. to determine the causes of asthenospermia; recommending treatments according to the causes of asthenozoospermia, empirical managements and artificial assisted reproduction. This consensus can provide expert consultation and advice for medical professionals engaged in reproductive medicine and andrology.

【Key words】 Asthenozoospermia; Diagnosis; Treatment; Expert consensus

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畸形精子症诊疗中国专家共识

中国医师协会生殖医学专业委员会生殖男科学组畸形精子症诊疗中国专家共识编写组

通信作者: 熊承良, Email: clxiong951@sina.com, 电话: +86-27-

82742288; 朱伟杰, Email: tzhuwj@jnu.edu.cn, 电话: +86-20-

85225718; 康跃凡, Email: fjkyl@163.com, 电话: +86-591-

87556044

【摘要】 畸形精子症是指精液中正常形态精子百分率低于正常参考值下限, 是男性不育症最常见的病因之一。中国医师协会生殖医学专业委员会生殖男科学组组织专家成立编写组起草本共识, 并经国内多位生殖男科专家审阅修订。本共识阐述了畸形精子症的定义、分类、病因、个体化治疗方案的选择以及患者的健康管理等, 旨在进一步规范畸形精子症的诊疗流程, 为从事生殖医学、男科学的专业医务人员提供专家咨询建议。

【关键词】 畸形精子症; 诊断; 治疗; 专家共识

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Chinese experts' consensus on the diagnosis and treatment of teratozoospermia

Chinese Expert Consensus Compilation Group for Teratozoospermia Diagnosis and Treatment, Reproductive Andrology Group, Reproductive Medicine Professional Committee of Chinese Medical Doctor Association

Corresponding authors: Xiong Chengliang, Email: clxiong951@sina.com, Tel: +86-27-82742288; Zhu Weijie, Email: tzhujw@jnu.edu.cn, Tel: +86-20-85225718; Kang Yuefan, Email: fjkyf@163.com, Tel: +86-591-87556044

【Abstract】 Teratozoospermia is defined as a decreased percentage of normal morphological sperm in the ejaculated semen compared to the limitation of the reference value. It is one of the most important causes of male infertility. This consensus was initiated by the Reproductive Andrology Group of the Chinese Association of Reproductive Medicine, and written by the consensus committee of reproductive andrological experts. The consensus was also reviewed by several other experts in male infertility. The present consensus focuses on the definition, classification, causes and the individualized treatment options of teratozoospermia, as well as the patient health management of teratozoospermia. This consensus will further standardize the diagnosis and treatment protocol of teratozoospermia, and provide professional consultations and advice for physicians in reproductive medicine and andrology.

【Key words】 Teratozoospermia; Diagnosis; Treatment; Expert consensus

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·临床研究·

浮游器筛选后精子超微结构变化和 IVF-ET 结局分析: 一项随机对照 试验

曹晓敏 刘丽 邸建永 刘烨 张美姿 徐凤琴

天津市第一中心医院生殖医学科 300192

通信作者: 徐凤琴, Email: xufengqin1968@126.com, 电话: +86-13652169698

【摘要】 目的 寻找体外受精 (*in vitro* fertilization, IVF) 过程中合适的精液处理方法。方法 本研究采用前瞻性随机对照双盲设计, 选取 300 例因女性因素且男性生育力检查未见异常行 IVF-胚胎移植 (embryo transfer, ET) 助孕的不孕夫妇为研究对象, 纳入的患者通过计算机产生随机数进行随机化分组, 分为浮游组 (新型无损伤精子筛选技术, FY 组, $n=100$)、密度梯度组 (DG 组, $n=100$) 和上游组 (SU 组, $n=100$)。收集三组患者受精后剩余的精子观察精子超微结构, 并比较三组优选后精子 DNA 碎片指数 (DNA fragment index, DFI) 及 IVF-ET 治疗过程中的受精率、卵裂率、优质胚胎率及妊娠率等指标之间的差异。结果 FY 组精子 DFI 显著低于 DG 组和 SU 组 ($3.22\% \pm 2.73\%$ 比 $8.31\% \pm 2.14\%$ 比 $6.43\% \pm 2.56\%$), 差异有统计学意义 ($P=0.02$), FY 组的精子头、尾部质膜完整率明显高于其他两组 ($92.0\% \pm 24.2\%$ 比 $80.2\% \pm 29.5\%$ 比 $73.2\% \pm 30.1\%$ 和 $93.9\% \pm 1.2\%$ 比 $80.1\% \pm 1.1\%$ 比 $74.9\% \pm 1.2\%$), 差异具有统计学意义 ($P=0.01$, $P=0.03$)。FY 组的优质胚胎率、囊胚形成率明显高于 DG 组和 SU 组 [44.14% ($452/1024$) 比 32.30% ($292/904$) 比 32.46% ($296/912$) 和 54.40% ($396/728$) 比 43.52% ($302/694$) 比 46.34% ($330/712$)] , 差异均具有统计学意义 (P 均 <0.001)。新鲜周期 FY 组的妊娠率和植入率明显高于 DG 组和 SU 组 [57.14% ($24/42$) 比 33.33% ($16/48$) 比 35.56% ($16/45$) 和 50.00% ($30/60$) 比 27.45% ($14/51$) 比 28.26% ($13/46$)] , 差异具有统计学意义 ($P=0.04$, $P=0.02$)。复苏周期 FY 组的妊娠率和植入率明显高于 DG 组和 SU 组 [52.38% ($22/42$) 比 31.25% ($10/32$) 比 37.14% ($13/35$) 和 52.38% ($22/42$) 比 29.41% ($10/34$) 比 30.56% ($11/36$)] , 差异具有统计学意义 ($P=0.03$, $P=0.02$)。结论 浮游法可减少对精子造成的物理损伤, 提高精子质膜的完整率, 降低精子 DFI, 改善辅助生殖技术结局。

【关键词】 密度梯度法; 上游法; 精子超微结构; 受精, 体外; 胚胎移植; 精子优选; 浮游法

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Influence of optimal selection of planktonic apparatus on sperm ultrastructure and IVF-ET outcome analysis: a randomized controlled trail

Cao Xiaomin, Liu Li, Di Jianyong, Liu Ye, Zhang Meizi, Xu Fengqin

Department of Reproductive Medicine, Tianjin First Central Hospital, Tianjin 300192, China

Corresponding author: Xu Fengqin, Email: xufengqin1968@126.com, Tel: +86-13652169698

【Abstract】 **Objective** To find a suitable semen treatment method in *in vitro* fertilization (IVF). **Methods** A prospective randomized double-blind design was performed, 300 infertile couples with female factors and no abnormal fertility

test were selected for IVF-embryo transfer (ET), the patients were randomly divided into float group (FY group, $n=100$), density gradient group (DG group, $n=100$) and upstream group (SU group, $n=100$). The remaining sperm after fertilization were collected from three groups, and sections of electron microscope were prepared. The ultrastructure of sperm was observed by transmission electron microscope. The differences among the three groups of selected sperm DNA fragment index (DFI) and fertilization rate, cleavage rate, high-quality embryo rate and pregnancy rate during IVF-ET were compared. **Results** The sperm DFI of the three groups after treatment was statistically different ($P=0.02$), and the sperm DFI of the FY group was significantly lower than that of DG group and SU group ($3.22\pm 2.73\%$ vs. $8.31\pm 2.14\%$ vs. $6.43\pm 2.56\%$). The rates of sperm head and tail plasma membrane integrity rate in FY group were significantly higher than those in the other two groups ($92.0\pm 24.2\%$ vs. $80.2\pm 29.5\%$ vs. $73.2\pm 30.1\%$ and $93.9\pm 1.2\%$ vs. $80.1\pm 1.1\%$ vs. $74.9\pm 1.2\%$), and the differences were statistically significant ($P=0.01$, $P=0.03$). The high-quality embryo rate and the blastocyst formation rate of FY group were significantly higher than those of DG group and SU group [44.14% ($452/1024$) vs. 32.30% ($292/904$) vs. 32.46% ($296/912$) and 54.40% ($396/728$) vs. 43.52% ($302/694$) vs. 46.34% ($330/712$)], and the differences were statistically significant (all $P<0.001$). The pregnancy rate and the implantation rate in the fresh cycle FY group were significantly higher than those in DG and SU groups [57.14% ($24/42$) vs. 33.33% ($16/48$) vs. 35.56% ($16/45$) and 50.00% ($30/60$) vs. 27.45% ($14/51$) vs. 28.26% ($13/46$)], and the differences were statistically significant ($P=0.04$, $P=0.02$). The pregnancy rate and implantation rate in the resuscitation cycle FY group were significantly higher than those in the DG and SU groups [52.38% ($22/42$) vs. 31.25% ($10/32$) vs. 37.14% ($13/35$) and 52.38% ($22/42$) vs. 29.41% ($10/34$) vs. 30.56% ($11/36$)], and the difference was statistically significant ($P=0.03$, $P=0.02$). **Conclusion** The Plankton method can reduce physical damage to sperm, improve the integrity rate of sperm plasma membrane and decrease sperm DFI, improve assisted reproductive technology outcome.

【Key words】 Density gradient method; Upstream method; Superstructure sperm ultrastructure; Fertilization *in vitro*; Embryo transfer; Sperm optimal plankton

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·临床研究·

早卵泡期长效长方案的胚胎移植策略

张俊韦 任炳楠 吴余玲 吴艳莉 胡继君 刘曼曼 孙丽君 王兴玲 管一春 杜明泽

郑州大学第三附属医院生殖医学科 450052

通信作者: 杜明泽, Email: 503047053@qq.com, 电话: +86-

15617679237

【摘要】 目的 探讨早卵泡期长效长方案的胚胎移植策略, 在获得较高活产率的同时降低多胎率。方法 采用回顾性队列研究, 分析 2017 年 1 月至 2019 年 2 月期间在郑州大学第三附属医院生殖医学科就诊的采用早卵泡期长效长方案助孕患者的临床资料。根据移植胚胎类型不同, 分为新鲜周期卵裂期胚胎移植组 (A 组)、新鲜周期囊胚移植组 (B 组)、冻融周期卵裂期胚胎移植组 (C 组)、冻融周期囊胚移植组 (D 组)。主要观察指标为活产率和多胎率。采用二元逻辑回归校正混杂因素。结果 A 组的中重度卵巢过度刺激综合征 (ovarian hyperstimulation syndrome, OHSS) 的发生率 [4.8% (110/2283)] 高于 C 组 [1.0% (6/614), $P<0.001$] 和 D 组 [2.1% (16/762), $P<0.001$]。B 组的中重度 OHSS 的发生率 [3.8% (42/1116)] 高于 C 组 ($P<0.001$)。移植 2 枚胚胎组的多胎率 [A 组 23.4% (535/2283) 和 C 组 20.8% (128/614)] 显著高于移植 1 枚囊胚组 [B 组 1.4% (16/1116) 和 D 组 0.9% (7/762)], 差异有统计学意义 ($P<0.001$)。B 组的临床妊娠率 [68.7% (767/1116)] 和活产率 [59.6% (665/1116)] 均高于 A 组 [63.5% (1449/2283), $P=0.003$; 54.8% (1250/2283), $P=0.008$]、C 组 [60.1% (369/614), $P<0.001$; 51.6% (317/614), $P=0.001$] 和 D 组 [62.7% (478/762), $P=0.007$; 52.8% (402/762), $P=0.003$], 而 A 组、C 组和 D 组间临床妊娠率和活产率的差异均无统计学意义 ($P>0.05$)。以 B 组为参照, 进行哑变量分析, A 组 ($aOR=0.86$, 95% $CI=0.74\sim0.99$, $P=0.044$)、C 组 ($aOR=0.76$, 95% $CI=0.62\sim0.93$, $P=0.008$) 及 D 组 ($aOR=0.79$, 95% $CI=0.65\sim0.95$, $P=0.013$) 的活产率均低于 B 组。结论 对于早卵泡期长效长方案, 在控制 OHSS 的基础上, 首选新鲜周期单囊胚移植, 在获得较高活产率的同时, 多胎率显著降低。

【关键词】 囊胚; 胚胎; 多胎; 活产率

Embryo transfer strategies of early follicular phase prolonged protocol

Zhang Junwei, Ren Bingnan, Wu Sheling, Wu Yanli, Hu Jijun, Liu Manman, Sun Lijun, Wang Xingling, Guan Yichun, Du Mingze

Reproductive Center of the Third Affiliated Hospital of Zhengzhou University, Zhengzhou 450052, China

Corresponding author: Du Mingze, Email: 503047053@qq.com, Tel: + 86-15617679237

【Abstract】 Objective To investigate the embryo transfer strategies of early follicular phase prolonged protocol, to reduce the risk of multiple birth rate while achieving a higher live birth rate. **Methods** It was a retrospective cohort study. Patients who underwent gonadotropin-releasing hormone (GnRH) agonist protocols in the Reproductive Center of the Third Affiliated Hospital of Zhengzhou University from January 2017 to February 2019 were included. According to the type of embryos transferred, we divided all cycles into four groups, fresh cycle cleavage stage embryo transfer group (group A), fresh cycle blastocyst transfer group (group B), freeze-thaw cleavage stage embryo transfer group (group C), freeze-thaw blastocyst transfer group (group D). The main outcome measures were live birth rate and multiple birth rate. Binary logistic regression was used to correct confounding factors. **Results** The risk of moderate to severe ovarian hyperstimulation syndrome (OHSS) in group A [4.8% (110/2283)] was higher than that in group C [1.0% (6/614), $P<0.001$] and group D [2.1% (16/762), $P<0.001$]. The risk of moderate to severe OHSS in group B [3.8% (42/1116)] was higher than that in group C ($P<0.001$). The multiple birth rate of the two embryos transfer group [group A 23.4% (535/2283), group C 20.8% (128/614)] was significantly higher than that of the one blastocyst transfer group [group B 1.4% (16/1116), group D 0.9% (7/762)], and the difference was statistically significant ($P<0.001$). The clinical pregnancy rate [68.7% (767/1116)] and the live birth rate [59.6% (665/1116)] of group B were higher than those of group A [63.5% (1449/2283), $P=0.003$; 54.8% (1250/2283), $P=0.008$], group C [60.1% (369/614), $P<0.001$; 51.6% (317/614), $P=0.001$] and group D [62.7% (478/762), $P=0.007$; 52.8% (402/762), $P=0.003$], but there was no statistical difference among group A, group C and group D. Taking group B as a reference, the live birth rate of group A ($aOR=0.86$, 95% $CI=0.74-0.99$, $P=0.044$), group C ($aOR=0.76$, 95% $CI=0.62-0.93$, $P=0.008$) and group D ($aOR=0.79$, 95% $CI=0.65-0.95$, $P=0.013$) was lower than that of group B. **Conclusion** For the early follicular phase prolonged protocol, based on the control of OHSS, fresh cycle single blastocyst transplantation is preferred. While obtaining a higher live birth rate, the multiple birth rate is significantly reduced.

【Key words】 Blastocyst; Embryo; Multiple birth; Live birth rate

·临床研究·

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孕早期子宫动脉血流动力学参数对反复妊娠丢失患者妊娠结局的预测价值

张敏 阮加里 Frempong Sophia Twum 鲍时华

同济大学附属第一妇婴保健院生殖免疫科, 上海 201204

通信作者: 鲍时华, Email: baoshihua@tongji.edu.cn, 电话: +86-

21-20261439

【摘要】 目的 探讨孕早期子宫动脉血流动力学参数监测对反复妊娠丢失 (recurrent pregnancy loss, RPL) 患者妊娠结局的预测价值。方法 回顾性分析 2017 年 11 月至 2018 年 5 月期间就诊于同济大学附属第一妇婴保健院生殖免疫科的 RPL 患者资料, 采用病例对照研究设计, 按照 RPL 妊娠结局将患者分为活产组和流产组, 分析两组患者在孕早期子宫动脉血流动力学参数的差异。结果 研究纳入活产组 348 例, 流产组 312 例。随孕周增加, 子宫动脉收缩期峰值/舒张末期流速 (peak uterine artery systolic/end-diastolic velocity, S/D)、搏动指数 (pulsatility index, PI) 及血流阻力指数 (blood flow resistance index, RI) 在两组中均呈下降趋势; 与流产组相比, 活产组子宫动脉 S/D、PI 和 RI 分别多下降 3.462 1 (95% CI=-6.483 5~0.440 8, $P=0.025$ 2)、0.474 2 (95% CI=-1.000 5~0.052 1, $P=0.078$ 1) 和 0.054 6 (95% CI=-0.111 5~0.002 4, $P=0.060$ 9), 孕早期活产组子宫动脉 S/D、PI 和 RI 下降速率较流产组高 0.064 5 (95% CI=0.013 6~0.115 9, $P=0.014$ 5)、0.009 4 (95% CI=0.000 5~0.018 4, $P=0.039$ 4) 和 0.001 1 (95% CI=0.000 1~0.002 0, $P=0.032$ 2)。结论 活产组子宫动脉血流参数下降速率较流产组更快, 早孕期监测子宫动脉血流动力学对 RPL 患者妊娠结局具有预测价值。

【关键词】 反复妊娠丢失; 子宫动脉血流; 妊娠结局; 病例对照研究
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Predictive value of uterine artery hemodynamic parameters in first trimester of pregnancy outcome in patients with recurrent pregnancy loss

Zhang Min, Ruan Jiali, Frempong Sophia Twum, Bao Shihua

Department of Reproductive Immunology, Shanghai First Maternity and Infant Hospital, Tongji University School of Medicine, Shanghai 201204, China

Corresponding author: Bao Shihua, Email: baoshihua@tongji.edu.cn, Tel: +86-21-20261439

【Abstract】 Objective To investigate the predictive value of uterine artery hemodynamic parameter monitoring in the first trimester on pregnancy outcomes in patients with recurrent pregnancy loss (RPL). **Methods** The RPL patients were selected from the Department of Reproductive and Immunology of Shanghai First Maternal and Infant Hospital between November 2012 and May 2018. RPL patients were divided into live birth group and miscarriage group according to their pregnancy outcome. Case-control studies were designed to compare the two groups in hemodynamic parameters of transvaginal ultrasonography-uterine artery during first trimester. **Results** Totally 348 cases in the live birth group and 312 cases in the miscarriage group were enrolled. As the gestational week increases, peak uterine artery systolic/end-diastolic velocity (S/D), pulsatility index (PI), and blood flow resistance index (RI) increased in both groups; compared with miscarriage group, uterine artery S/D, PI, and RI of live birth group decreased by 3.462 1 (95% $CI=-6.483\ 5-0.440\ 8$, $P=0.025\ 2$), 0.474 2 (95% $CI=-1.000\ 5-0.052\ 1$, $P=0.078\ 1$), and 0.054 6 (95% $CI=-0.111\ 5-0.002\ 4$, $P=0.060\ 9$), respectively. Uterine artery S/D, PI, RI slope rates in live birth group were 0.064 5 (95% $CI=0.013\ 6-0.115\ 9$, $P=0.014\ 5$), 0.009 4 (95% $CI=0.000\ 5-0.018\ 4$, $P=0.039\ 4$), and 0.001 1 (95% $CI=0.000\ 1-0.002\ 0$, $P=0.032\ 2$) higher than those in miscarriage group during early pregnancy. **Conclusion** The slope rate of uterine arterial blood flow parameters in live birth group is faster than that in miscarriage group. Monitoring of uterine arterial blood flow during the first trimester may have a predictive value for pregnancy outcomes in RPL patients.

【Key words】 Recurrent pregnancy loss; Uterine arterial blood flow; Pregnancy outcome; Case-control study

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·临床报道·

早期妊娠丢失患者全身性和母-胎界面的氧化应激水平研究

弓弦 王建梅 孙丽 黎小佩 张钰娟

天津医科大学第二医院计划生育科 300211

通信作者: 张钰娟, Email: zhangyj@tmu.edu.cn, 电话: +86-22-

88329025

【摘要】 目的 了解早期妊娠妇女全身性与母-胎界面局部氧化应激状态的相关性及各氧化应激指标的影响因素,探究早期妊娠丢失(early pregnancy loss, EPL)与脂质过氧化及总抗氧化能力(total antioxidant capacity, T-AOC)生物标志物之间的关联。方法 采用病例对照研究,于2017年12月至2018年7月期间在天津医科大学第二医院计划生育科招募 EPL 病例组和正常早期妊娠人工流产对照组为研究对象(每组各103例),检测两组患者血清及妊娠绒毛组织的丙二醛(malondialdehyde, MDA)和 T-AOC 水平(血清检测每组各103例,绒毛组织检测每组各60例)。分析各标志物的影响因素及其在血清和绒毛组织中含量的相关性,比较两组间各标志物水平的差异。结果 病例组绒毛 MDA、T-AOC 及对照组绒毛 MDA、T-AOC 均与其血清标志物含量呈正相关,相关系数分别为 $r=0.744$, $P<0.001$; $r=0.312$, $P=0.015$; $r=0.712$, $P<0.001$; $r=0.650$, $P<0.001$ 。除病例组绒毛 MDA 外,两组血清和对照组绒毛 MDA 及 T-AOC 均随妊娠时间的增加而升高。病例组的妊娠时间每增加1周,血清 MDA 增加 8.3% ($P=0.005$),血清 T-AOC 增加 4.2% ($P=0.002$),绒毛 T-AOC 增加 2.6% ($P=0.010$),差异均有统计学意义;对照组的妊娠时间每增加1周,血清 MDA 增加 11.3% ($P=0.004$),血清 T-AOC 增加 5.4% ($P=0.007$),绒毛 MDA 增加 18.7% ($P=0.017$),绒毛 T-AOC 增加 8.4% ($P=0.009$)。调整妊娠时间后,病例组血清 T-AOC 比对照组低 13.4% ($P<0.001$),绒毛 T-AOC 比对照组低 33.7% ($P<0.001$),绒毛 MDA 比对照组高 30.1% ($P=0.012$),两组血清 MDA 的差异无统计学意义。结论 早期妊娠妇女全身性氧化应激状态与母-胎界面同步,妊娠时间是影响血清和绒毛组织氧化应激水平的重要因素,EPL 与孕妇全身性和母-胎界面抗氧化能力降低以及母-胎界面脂质过氧化损伤有关。

【关键词】 流产,稽留; 流产,自然; 氧化性应激; 血清; 绒毛膜绒毛; 脂质过氧化; 抗氧化能力

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Levels of systemic and maternal-fetal interface oxidative stress in women with early pregnancy loss

Gong Xian, Wang Jianmei, Sun Li, Li Xiaopei, Zhang Yujuan

Department of Family Planning, the Second Hospital of Tianjin Medical University, Tianjin 300211, China

Corresponding author: Zhang Yujuan, Email: zhangyj@tmu.edu.cn, Tel: +86-22-88329025

【Abstract】 Objective To understand the correlation between systemic and local (at the maternal-fetal interface) oxidative stress in women with early pregnancy and the influencing factors of indicators, and to explore the associations

between early pregnancy loss (EPL) and biomarkers of lipid peroxidation and total antioxidant capacity (T-AOC). **Methods** A case-control study was performed. From December 2017 to July 2018, cases of EPL and controls of normal early pregnant women requesting induced abortions due to unintended pregnancies were recruited in the Family Planning Department of the Second Hospital of Tianjin Medical University. The levels of malondialdehyde (MDA) and T-AOC in serum of 103 participants and chorionic villous tissue of 60 participants in each group were measured. The influencing factors and the correlations between the levels of each biomarker in serum and villous were analyzed. The differences in the levels of each biomarker between the two groups were compared. **Results** The levels of MDA and T-AOC in villi of case group and control group were both positively correlated with their serum markers, their correlation coefficients were $r=0.744$, $P<0.001$; $r=0.312$, $P=0.015$; $r=0.712$, $P<0.001$; $r=0.650$, $P<0.001$, respectively. Except for villus MDA in case group, serum and villus MDA and T-AOC increased with the increasing of gestational days in both groups. For each additional week of gestation in case group, serum MDA increased by 8.3% ($P=0.005$), serum T-AOC increased by 4.2% ($P=0.002$), villus T-AOC increased by 2.6% ($P=0.010$), all of which were statistically significant; in control group, the serum MDA, serum T-AOC, villus MDA and villus T-AOC increased by 11.3% ($P=0.004$), 5.4% ($P=0.007$), 18.7% ($P=0.017$) and 8.4% ($P=0.009$) respectively for each additional week of gestation. After adjusting the gestational days, the serum T-AOC of the case group was 13.4% lower than that of control group ($P<0.001$), the villus T-AOC was 33.7% lower than that of control group ($P<0.001$), while the villus MDA was 30.1% higher than that of control group ($P=0.012$). The serum MDA of the two groups had no statistic significance. **Conclusion** The status of systemic oxidative stress is synchronized with that in the maternal-fetal interface in early pregnant women. Gestational age is an important factor affecting oxidative stress in serum and villous. EPL is associated with the reduction of systemic and maternal-fetal interface antioxidant capacity and maternal-fetal interface lipid peroxidation damage.

【Key words】 Abortion, missed; Abortion, spontaneous; Oxidative stress; Serum; Chorionic villi; Lipid peroxidation; Antioxidant capacity

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·临床报道·

误诊为宫内孕的宫颈妊娠 11 例临床分析

张媛媛 陈雁鸣

首都医科大学附属北京妇产医院生殖调节/计划生育科 100006

通信作者: 陈雁鸣, Email: chenym69@126.com, 电话: +86-10-52277236

【摘要】 目的 总结误诊为宫内孕的宫颈妊娠病例临床与超声影像学特征, 以提高临床医师对宫颈妊娠早期诊断的能力。方法 回顾性分析 2010 年 1 月至 2019 年 12 月期间首都医科大学附属北京妇产医院生殖调节/计划生育科收治的 11 例误诊为宫内孕的宫颈妊娠患者生育史、专科查体、误诊前后的超声影像学特征及治疗结局。结果 11 例病例中已育者 7 例, 其中有剖宫产史 6 例; 9 例有流产刮宫术史; 误诊为宫内早孕 6 例, 误诊为稽留流产 3 例, 误诊为难免流产 2 例, 其中误诊时行药物流产或刮宫术 8 例, 4 例出现大出血。9 例行子宫动脉栓塞术; 6 例行宫腔镜明确诊断及手术; 平均住院 6 d, 术后血 β -人绒毛膜促性腺激素 (human chorionic gonadotropin, hCG) 恢复正常中位时间为 20 d。结论 宫颈妊娠临床症状不典型, 超声检查是主要的诊断依据, 早期妊娠超声影像学提示是误诊主要原因, 动态观察超声特征可帮助早期识别宫颈妊娠。

【关键词】 误诊; 宫颈妊娠; 超声检查

Clinical analysis of 11 cases of cervical pregnancy misdiagnosed as intrauterine pregnancy

Zhang Yuanyuan, Chen Yanming

Department of Reproductive Management, Beijing Obstetrics and Gynecology Hospital, Capital Medical University, Beijing 100006, China

Corresponding author: Chen Yanming, Email: chenym69@126.com, Tel: +86-10-52277236

【Abstract】 Objective To summarize the clinical characteristics of cervical pregnancy misdiagnosed as intrauterine pregnancy and improve the ability of clinicians in early diagnosis of cervical pregnancy. **Methods** Eleven cases of cervical pregnancy misdiagnosed as intrauterine pregnancy were retrospectively analyzed in Department of Reproductive Management in Beijing Obstetrics and Gynecology Hospital of Capital Medical University. **Results** Among the 11 patients, 7 were fertile and 4 were infertile; 9 cases had a history of abortion and curettage; 6 cases were misdiagnosed as early intrauterine pregnancy, 3 cases as delayed abortion, 2 cases as inevitable abortion, among which 8 cases were misdiagnosed as medical abortion or curettage, and 4 cases had massive hemorrhage. Nine patients

underwent uterine artery embolization. Six patients were definitely diagnosed and operated by hysteroscopy. The mean hospitalization was 6 d, and postoperative β -human chorionic gonadotropin (hCG) returned to normal for a median time of 20 d.

Conclusion Clinical symptoms of cervical pregnancy are atypical, and ultrasound examination is the main diagnostic basis. Ultrasound imaging hints of early pregnancy are the main cause of misdiagnosis. Dynamic observation of ultrasonic signs can help to identify cervical pregnancy at early stage.

【Key words】 Misdiagnose; Cervical pregnancy; Ultrasound examination

·个案报道·

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子宫内膜癌卵巢组织冻存自体移植 1 例报道

阮祥燕¹ 程姣姣¹ 杜娟¹ 李扬璐¹ 金凤羽¹ 卢丹¹ 周蓉² 代

荫梅¹ 周琦¹ Matthias Korell³ 王虎生¹ 谷牧青¹ Alfred O.

Mueck⁴

¹ 首都医科大学附属北京妇产医院 100026; ² 北京大学人民医院

100044; ³ 德国诺伊斯约翰娜艾蒂安医院 41462; ⁴ 德国图宾根大学妇

产医院内分泌与绝经中心 72076

通信作者: 阮祥燕, Email: ruanxiangyan@ccmu.edu.cn, 电话: +86-

13011215678

【摘要】 目的 通过卵巢组织冻存及自体移植手术保护子宫内膜癌患者生育力与卵巢内分泌功能。方法 对 1 例 33 岁子宫内膜癌 I 期患者在癌症手术过程中进行卵巢组织取材、冻存, 待其癌症完全缓解后进行冻存卵巢组织自体移植手术, 随访监测患者的激素水平、卵泡发育情况以及绝经相关症状。结果 卵巢组织移植 1 个月后, 改良 Kupperman 评分由 12 分降低至 2 分, 绝经相关症状基本消失, 移植第 2 个月卵泡刺激素降低至 21.78 IU/L, 雌二醇由<13.76 ng/L 升高至 65.55

ng/L, B 超监测到有卵泡发育。移植第 4 个月, 卵泡刺激素降至 6.26 IU/L, 雌二醇水平升至 112.22 ng/L, 移植后第 9 个月, 雌二醇水平为 118.14 ng/L, 孕酮水平升高至 8.96 μg/L, 且 B 超下监测到 2 个排卵后黄体。结论 卵巢组织冻存移植 2 个月后卵巢功能恢复, 证明卵巢组织在临床上移植成功。

【关键词】 卵巢组织冻存; 卵巢组织移植; 子宫内膜癌; 卵巢排卵; 卵巢功能

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A case report of cryopreserved ovarian tissue retransplantation in endometrial cancer

Ruan Xiangyan¹, Cheng Jiaojiao¹, Du Juan¹, Li Yanglu¹, Jin Fengyu¹, Lu Dan¹, Zhou Rong², Dai Yinmei¹, Zhou Qi¹, Matthias Korell³, Wang Husheng¹, Gu Muqing¹, Alfred O. Mueck⁴

¹ Beijing Obstetrics and Gynecology Hospital, Capital Medical University, Beijing 100026, China; ² Peking University People's Hospital, Beijing 100044, China; ³ Johanna-Etienne Hospital in Neuss, Neuss 41462, Germany; ⁴ Section of Endocrinology and Menopause, Department of Women's Health, University of Tuebingen, Tuebingen 72076, Germany

Corresponding author: Ruan Xiangyan, Email: ruanxiangyan@ccmu.edu.cn, Tel: +86-13011215678

【Abstract】 **Objective** To preserve fertility and endocrine function of an endometrial carcinoma patient by ovarian tissue cryopreservation and transplantation. **Methods** Part of the ovary was harvested and cryopreserved when surgery for a 33-year-old woman who was diagnosed with endometrial carcinoma. After the cancer reached remission, the patient underwent cryopreserved ovarian tissue transplantation. The endocrine hormone, follicle growth, and menopausal syndromes were detected. **Results** One month after the surgery of transplantation, the modified Kupperman scores decreased from 12 to 2, and the menopausal syndrome disappeared. Two months after the operation of transplantation, the concentration of follicle-stimulating hormone (FSH) decreased to 21.78 IU/L, the level of estradiol increased from 13.76 ng/L to 65.55 ng/L, and follicle growth was observed by ultrasound. Four months after the surgery of transplantation, the level of FSH decreased to 6.26 IU/L, the level of estradiol increased to 112.22 ng/L. Nine months after the operation of transplantation, the level of estradiol was 118.14 ng/L, the level of progesterone increased to 8.96 μg/L, and two corpus luteum after ovulation were detected by ultrasound. **Conclusion** Two months after the surgery of transplantation, the ovarian function has returned to normal, which demonstrated the success of transplantation of frozen-thawed ovarian tissue.

【 Key words 】 Ovarian tissue cryopreservation; Ovarian tissue transplantation; Endometrial cancer; Ovarian ovulation; Ovarian function

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·个案报道·

NTRK1 基因新发突变致遗传性感觉和自主神经病 4 型的遗传学分析及出生缺陷阻断研究

宋菲 陈大蔚 周平 魏兆莲 曹云霞

安徽医科大学第一附属医院妇产科, 合肥 230022

通信作者: 曹云霞, Email: caoyunxia6@126.com, 电话: +86-551-

65908421

【摘要】 目的 探讨基于二代测序的植入前单体型分析在遗传性感觉和自主神经病 4 型 (hereditary sensory and autonomic neuropathy IV, HSAN IV) 出生缺陷阻断中的应用价值。方法 纳入 1 个 HSAN IV 家系, 采用高通量测序和 Sanger 测序相结合的方法对 *NTRK1* 基因进行突变分析, 通过构建 TrkA 表达载体对突变进行致病性预测。对活检的囊胚滋养层细胞进行全基因组扩增, 选择致病基因上下游数十至数百个单核苷酸多态性位点作为连锁遗传标记, 通过基于二代测序的植入前单体型分析完成植入前遗传学检测。结果 先证者 *NTRK1* 基因存在复合杂合突变, 包括新发现的移码突变 (c.963delG; p.Val321-Valfs*149) 和已报道的错义突变 (c.850+1G>A), 新突变可导致编码蛋白截短与功能失调, 其母亲和

父亲分别为上述突变携带者。经植入前遗传学检测，活检的 2 个囊胚中 1 个携带母方致病基因，1 个受累。选择携带母方致病基因的胚胎进行移植，未获妊娠。结论 本研究是我国 *NTRK1* 基因突变行植入前遗传学检测的首例报道，新发现的 c.963delG 突变丰富了 *NTRK1* 基因的突变谱，同时为阻断单基因遗传病出生缺陷的发生提供有效的预防手段。

【关键词】 遗传性感觉和自主神经病 4 型； 先天性无痛无汗症； *NTRK1* 基因； 植入前遗传学检测

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Preimplantation genetic testing and birth defect prevention of hereditary sensory and autonomic neuropathy IV caused by novel *NTRK1* mutation

Song Fei, Chen Dawei, Zhou Ping, Wei Zhaolian, Cao Yunxia

Department of Obstetrics and Gynecology, the First Affiliated Hospital of Anhui Medical University, Hefei 230022, China

Corresponding author: Cao Yunxia, Email: caoyunxia6@126.com, Tel: +86-551-65908421

【Abstract】 Objective To explore the application of next generation sequencing (NGS)-based single nucleotide polymorphism (SNP) haplotyping of preimplantation genetic testing for monogenic (PGT-M) in the prevention of hereditary sensory and autonomic neuropathy IV (HSAN IV). **Methods** A Chinese family of HSAN IV was enrolled in this study. NGS and Sanger sequencing were combined to conduct mutational analysis of *NTRK1* gene. Functional evaluation of mutation was performed through the cloning of expression construct. After whole genome amplification of biopsied trophoctoderm cells, some high-frequency SNP markers were selected for NGS-based haplotyping, including SNPs located upstream and downstream of *NTRK1* target region. **Results** Two compound heterozygous mutations of the *NTRK1* gene, the previously reported mutation c.850+1G>A and the novel frameshift mutation (c.963delG; p.Val321-Valfs*149), were identified in the proband, inherited from maternal and paternal sides, respectively. The novel frameshift mutation created a new reading frame, leading to dysfunctional and truncated protein. According to the PGT-M results, one of the blastocysts, inherited the maternal pathogenic allele and the paternal normal allele, was thawed and transferred. While the other blastocyst inherited both pathogenic allele. Unfortunately, there was no subsequent pregnancy. **Conclusion** This is the first report of preimplantation genetic testing of *NTRK1* gene mutations in China. The novel frameshift mutation c.963delG expands the gene mutation spectrum of HSAN IV. NGS-based SNP haplotyping applied in PGT-M provides an effective way to prevent birth defects of single-gene inherited diseases.

【Key words】 Hereditary sensory and autonomic neuropathy IV; Congenital insensitivity to pain with anhidrosis; *NTRK1* gene; Preimplantation genetic testing

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·综述·

宫腔灌注 hCG 对胚胎着床影响的研究进展

肖奇梦 刘源 孙翟 陈佩琴 傅悦 柏明珠 张箴波

上海交通大学附属第一人民医院辅助生殖中心 200080

通信作者: 张箴波, Email: zhangzhenbozzb@shsmu.edu.cn, 电话:

+86-15921516760

【摘要】 由于各种因素的影响, 不孕发生率在逐年增高。体外受精-胚胎移植 (*in vitro* fertilization-embryo transfer, IVF-ET) 技术使不孕夫妇的生育愿望成为可能, 然而着床失败一直阻碍着 IVF-ET 技术的发展。着床的过程十分复杂, 胚胎质量、子宫内膜容受性是成功着床的关键, 其中人绒毛膜促性腺激素 (human chorionic gonadotropin, hCG) 在着床过程甚至整个妊娠过程中起到重要作用。而目前关于胚胎移植前灌注 hCG 是否会影响患者的妊娠结局, 存在两种观点: 宫腔灌注 hCG 能改善患者的妊娠结局; 宫腔灌注 hCG 可能不仅不会改善患者妊娠率, 甚至会给患者带来不良后果。但是由于已完成的研究中没有较为统一的标准, 使得宫腔灌注 hCG 与胚胎着床之间的关系仍没有确切定论。本文对国内外宫腔灌注 hCG 和胚胎着床关系的研究进展进行了综述。

【关键词】 宫腔灌注; 人绒毛膜促性腺激素; 胚胎着床

Research progress on the effect of intrauterine infusion of hCG on embryo implantation

Xiao Qimeng, Liu Yuan, Sun Di, Chen Peiqin, Fu Yue, Bai Mingzhu, Zhang Zhenbo

Reproductive Medicine Center, Shanghai General Hospital, Shanghai Jiao Tong University, Shanghai 200080, China

Corresponding author: Zhang Zhenbo, Email: zhangzhenbozzb@shsmu.edu.cn, Tel: +86-15921516760

【Abstract】 Due to various factors, the proportion of infertile couples is increasing. *In vitro* fertilization-embryo transfer (IVF-ET) technology has made it possible for infertile couples to give birth. However, implantation failure has always hindered the development of IVF-ET. Embryo quality and endometrial receptivity are the keys to successful implantation. The implantation process is complicated and involves a variety of cytokines. Among them, human chorionic gonadotropin (hCG) plays an important role in the implantation process and even the entire pregnancy. At present, there are two opinions about whether hCG perfusion before embryo

transfer affects the patient's pregnancy outcome: intrauterine infusion of hCG can improve the patient's pregnancy outcome; intrauterine infusion of hCG may not only not improve the patient's pregnancy rate, and even bring adverse consequences to the patient. But because there is no more uniform standard in the completed researches, the relationship between intrauterine infusion of hCG and embryo implantation is still inconclusive. Now, we summarize their contributions in this paper.

【 Key words 】 Intrauterine infusion; Human chorionic gonadotropin; Embryo implantation

·综述·

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不同来源的间充质干细胞及其外泌体治疗早发性卵巢功能不全的作用及机制研究进展

赵馨扬 谭季春

中国医科大学附属盛京医院妇产科生殖医学中心/辽宁省生殖障碍疾病与生育力重塑重点实验室, 沈阳 110022

通信作者: 谭季春, Email: tjczjh@163.com, 电话: +86-18940251868

【摘要】 早发性卵巢功能不全 (premature ovarian insufficiency, POI) 是一种严重影响育龄妇女生殖健康和生活质量的内分泌疾病, 目前尚无有效的恢复卵巢功能的治疗手段。近年来很多研究表明, 不同来源的间充质干细胞 (mesenchymal stem cells, MSC) 通过改善卵巢组织微环境、免疫调节、促进卵泡发育、抑制颗粒细胞凋亡等, 恢复 POI 患者的卵巢功能及生育能力。本文综述了 POI 的治疗方法研究现状、不同来源的 MSC 及其外泌体治疗 POI 的可能性评估及机制的研究进展。

【关键词】 间充质干细胞; 早发性卵巢功能不全; 外泌体; 颗粒细胞
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Progress in the study of the effect and mechanism of different mesenchymal stem cells and their exosomes in the treatment of premature ovarian insufficiency

Zhao Xinyang, Tan Jichun

Center of Reproductive Medicine, Department of Obstetrics and Gynecology, Shengjing Hospital of China Medical University/Key Laboratory of Reproductive Disorders and Fertility Remolding, Liaoning Province, Shenyang 110022, China

Corresponding author: Tan Jichun, Email: tjczjh@163.com, Tel: +86-18940251868

【Abstract】 Premature ovarian insufficiency (POI) is an endocrine disease that seriously affects reproductive health and life quality of women of childbearing age. At present, there is no effective treatment to restore ovarian function. In recent years, many studies have shown that different sources of mesenchymal stem cells (MSC), cytokines and exosomes secreted by MSC can restore the ovarian function and fertility of POI patients by improving the microenvironment of ovarian tissue, immunomodulation, promoting follicular development, inhibiting granulosa cell apoptosis and so on. This article reviewed the current status of the treatment of POI, the possibility assessment and mechanism of different MSC and their exosomes.

【Key words】 Mesenchymal stem cell; Premature ovarian insufficiency; Exosome; Granulosa cell

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