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基础窦卵泡数对 IVF/ICSI-ET 超排卵周期卵巢反应的预测价值*

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摘要 目的: 窦卵是女性宫腔内的泡状细胞,与女性卵巢的发育及功能密切相关。本研究针对体外受精(IVF)周期中基础窦卵泡数(antral follicle count, AFC)的变化情况,探讨 AFC 对卵巢反应的预测价值,为临床研究提供理论基础。**方法:** 回顾性分析 2012 年 1 月至 2012 年 12 月在我院生殖医学中心接受体外受精-胚胎移植的 157 例患者的临床资料,根据基础窦卵泡数将所选病例分为 A 组($bAFC \geq 10$)和 B 组($bAFC < 10$)。对比并分析两组研究对象的促性腺激素(Gn)的用量及使用时间、获卵数、人绒毛膜促性腺激素(HCG)注射日的血清中雌激素(E2)水平、受精率、临床妊娠率等。**结果:** A 组患者的 Gn 用量、HCG 日 E2 值、获卵数及临床妊娠率均显著高于 B 组,差异具有统计学意义($P < 0.05$);两组患者的年龄和基础卵泡刺激素水平差异显著且具有统计学意义($P < 0.05$);两组患者的不孕原因、不孕年限及助孕方式无明显差异($P > 0.05$)。**结论:** 基础窦卵泡对体外受精女性促排卵周期的卵巢反应及助孕结局具有一定的预测价值,其数量的多少可作为促排卵过程中评价卵巢反应性的参考指标,应在临床进一步推广。

关键词: 窦卵泡; 体外受精; 卵巢反应; 促排卵

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Prediction Values of bAFC on the Response to Ovary in the IVF/ICSI-ET Super Ovulation Cycle*

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ABSTRACT Objective: The antral follicles are the intrauterine alveolar cells which is closely relative to the ovary growth and function of females. This study aims to exploring the predictive value for ovarian response by means of observing the changes of AFC levels during the *in vitro* fertilization (IVF) cycle so as to provide a theoretical basis for clinical research. **Methods:** A retrospective analysis was performed on the clinical data of 157 patients who were accepted the IVF-ET at the center of reproductive medicine in our hospital from January 2012 to December 2012. According to the bAFC, the selected patients were divided into two groups, namely, the group A($bAFC \geq 10$) and group B ($bAFC < 10$). Then the time and dose of Gn, the numbers of ovum, the levels of E2 in serum on the date of HCG injection, the rate of fertilization and pregnancy in the two groups were compared and evaluated. **Results:** The dose of Gn, the numbers of ovum, the levels of E2 in serum on the date of HCG injection and the rate of pregnancy in group A were higher than those of the group B with statistically significant differences($P < 0.05$); there were statistically significant differences about the age and the quantity of bAFC in the two groups ($P < 0.05$); but there was no significant difference about the reasons and time of infertility and the assistant methods for pregnancy in the two groups ($P > 0.05$). **Conclusions:** It is suggested that the quantity of bAFC could predict the functions of women's ovary for those who were taken the *in vitro* fertilization and it might become an essential indicator in the future for the clinical to detect the ovarian reactions of the infertile females during the super ovulation cycles.

Key words: Antral follicle; *In vitro* fertilization (ivf); Ovarian response; Stimulated ovulation

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前言

近年来,体外受精-胚胎移植(*in vitro* fertilization-embryo transfer, IVF-ET)技术被广泛应用于不孕不育症的临床治疗中,

并获得了良好的效果。但是,体外受精的成功率也受到一些因素的影响,其中女性不孕患者在超排卵过程中的卵巢反应性较差是一项重要因素^[1,2]。卵巢作为女性的重要器官,具有生殖和分泌性激素的功能,女性卵巢的功能直接影响着女性的生育能

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力。窦卵泡是反映卵巢储备的一项重要指标^[3-5]。因此,在患者进入 IVF 促排卵周期之前,根据其基础窦卵泡数对卵巢储备功能进行预测评估有助于帮助医生选择治疗方案以及提高获卵数及临床妊娠率^[6]。本研究对 157 例女性不孕患者的经阴道超声窦卵泡计数(antral follicle count, AFC)进行回顾性分析,探讨促排卵周期中窦卵泡数对卵巢反应性的预测价值,为更好的选择个体化治疗方案、获得更好的临床妊娠结局提供依据。

1 资料与方法

1.1 研究对象

选取 2012 年 1 月 1 日 - 2012 年 12 月 31 日在我院生殖医学中心接受 IVF/ICSI-ET 的患者 157 例。患者年龄分布在 25-45 岁,平均年龄 32.78 ± 5.13 岁;基础窦卵泡数 2-42 个,平均 12.7 ± 3.4 个;不孕年限为 1-12 年,平均 5.08 ± 2.91 年。不孕原因:女性输卵管因素,如子宫内异症、排卵障碍等;男性因素,如严重少弱精子症、无精子症及逆行射精等;其他因素,如多次人工授精失败等。根据基础 AFC 值,将基础窦卵泡数 ≥ 10 个的患者作为 A 组,基础窦卵泡数 < 10 个的患者作为 B 组(含取卵失败或放弃治疗者)。

1.2 研究方法

1.2.1 卵泡的监测^[7] 采用东芝 Ssa-240 a 黑白超声诊断仪,探头频率 5.0-7.5 MHz,于月经周期的第 2 天上午行阴道 B 超检查,计数直径为 2-8 mm 的窦卵泡数量。所有检查均由同一位具有 5 年生殖医学临床经验的医师操作,以确保结果的一致性。

1.2.2 促排卵方案^[8] 于前次月经黄体中期(即长周期)或后次月经周期第 2 天(即短周期)给与 $100 \mu\text{g}$ /支的 GnRH 抑制剂进行降调节;月经周期第 3 天用 75 uFSH 促性腺激素;根据卵泡

的生长情况和血清中雌激素的水平调整用药剂量,对于生长缓慢的卵泡给予促性腺激素;当双侧卵巢出现直径 $\geq 18 \text{ mm}$ 且血雌激素浓度 $\geq 1000 \text{ pg/ml}$ 的卵泡发育达 3 个或以上时,给予肌注 10000 IU 的人绒毛膜促性腺激素 HCG,36 小时后取卵。

1.2.3 IVF-ET^[9] 常规体外受精及早期胚胎培养,记录胚胎发育情况。取卵后的第 3 天行胚胎移植,移植后的 14 天行妊娠试验,7 周后经 B 超检查有胎心搏动者则认定为临床妊娠。

1.3 观察指标

观察两组患者的促性腺激素(Gn)的用量及使用时间、获卵数、人绒毛膜促性腺激素(HCG)注射日血清中雌激素(E2)的含量、受精率及临床妊娠率等。

1.4 统计学处理

采用 SPSS19.0 软件进行统计处理,各样本均值比较采用 t 检验,结果以均数 $\pm$ 标准差($\bar{x} \pm s$)表示,计数资料以百分率表示并用 χ^2 检验,以 $P < 0.05$ 为差异具有统计学意义。

2 结果

2.1 两组患者的临床资料

如表 1 所示,A 组共 78 例患者,其中 48 例为原发性不孕,30 例为继发性不孕;平均年龄为(30.06 ± 3.50)岁;不孕时间为(4.0 ± 5.26)年;bFSH 为(7.21 ± 1.86) IU/L;36 例采用体外受精,42 例采用单精子注射。B 组共 79 例患者,其中 42 例为原发性不孕,37 例为继发性不孕;平均年龄为(35.35 ± 5.19)岁;不孕时间为(5.07 ± 5.36)年;bFSH 为(9.56 ± 3.56) IU/L;28 例采用体外受精,51 例采用单精子注射。两组患者的不孕原因、年限及助孕方式无明显差异($P > 0.05$);但两组患者的年龄和基础卵泡刺激素水平差异显著,具有统计学意义($P < 0.05$)。

表 1 bAFC 值不同的两组患者的一般资料

Table 1 General data of the patients with different bAFC of the two groups

Groups	Case	Age (year)	Methods(case)		Infertility factors(case)		Course	bFSH(IU/L)
			IVF	ICSI	Primary	Secondary		
A(AFC ≥ 10)	78	30.06 ± 3.50	36	42	48	30	4.0 ± 5.26	7.21 ± 1.86
B(AFC < 10)	79	35.35 ± 5.19	28	51	42	37	5.07 ± 5.36	9.56 ± 3.56

2.2 两组超排卵周期的卵巢反应情况

如表 2 所示,A 组 Gn 用量为(30.55 ± 9.90) IU;使用时间为(11.20 ± 4.89)天;获卵数为(20.80 ± 10.42)个;HCG 日 E2 值为(26516.13 ± 14928.85);受精率为 86%;临床妊娠率为 48%。B 组 Gn 用量为(40.53 ± 16.9) IU;使用时间为(10.54 ± 3.85)天;获卵数为(9.00 ± 6.53)个;HCG 日 E2 值为(14437.03 ± 10207.64);

受精率为 84%;临床妊娠率为 20%。两组患者 Gn 使用时长和受精率差异无统计学意义($P > 0.05$);A 组患者的 Gn 用量、HCG 日 E2 值、获卵数及临床妊娠率均显著高于 B 组,差异具有统计学意义($P < 0.05$)。结果表明,患者的基础窦卵泡数越多,其获卵数和临床妊娠率就越高。

表 2 两组产妇不良反应发生情况

Table 2 Incidence of adverse reactions

Group	Gn level(IU)	Time(day)	Ovum	E ₂	Fertilization(%)	Pregnancy(%)
A ≥ 10	30.55 ± 9.90	11.20 ± 4.89	20.80 ± 10.42	26516.13 ± 14928.85	86%	48%
B < 10	40.53 ± 16.9	10.54 ± 3.85	9.00 ± 6.53	14437.03 ± 10207.64	84%	20%

Note: compared between two groups, $P < 0.05$.

3 讨论

卵巢储备功能是指卵巢皮质内原始卵泡生长发育成为可受精卵母细胞的能力,女性的生育潜能会随着年龄的增长而逐年下降,36岁以后尤为明显^[10,11]。有研究证实,随着患者年龄的增长,其获卵数、受精率、种植率及临床妊娠率等都会明显降低^[12]。窦卵泡的数目与卵巢的反应性密切相关。相关研究显示,女性患者月经期第2天的基础窦卵泡数小于等于4个或卵巢体积小于等于3立方米,亦或二者并存时,人工授精(IVF)促排卵周期的取消率呈上升趋势,而获卵数及妊娠率则明显降低。因此,认为窦卵泡数是预测卵巢低反应性的最佳指标^[13-15]。从原始卵泡生长到进入窦卵泡阶段,窦前卵泡均不依赖促性腺激素的刺激,当受到足够量的促性腺激素刺激时,将使得大量窦卵泡发育成熟,如在IVF周期中,果纳芬一类促性腺激素启动对窦卵泡的募集^[18,19]。由此可见,窦卵泡的数目可以较直观地反映卵巢的储备能力,而卵巢的储备能力与超排卵药物的反应、获卵数及IVF妊娠结局密切相关。此外,卵巢反应较差的患者多数需要给予更大剂量的促性腺激素进行促排卵,但用药期间发生卵巢过度刺激等并发症的发生率也随之增高。另有研究显示,IVF中开始进行促排卵前,经超声检查窦卵泡数不足5个的患者无一例成功妊娠^[16]。还有研究显示,bAFC与患者的年龄、基础bFSH、Gn用量、获卵数之间存在一定的相关性,当基础窦卵泡数不超过3个时,患者的周期取消率高达68.8%^[17]。

本研究回顾性分析了157例不孕患者的临床资料发现,卵巢反应正常的患者的窦卵泡数明显高于卵巢反应差的患者。结果提示我们,在进行IVF-ET前,对患者的卵巢反应进行正确的预测和评价有助于掌握患者的卵巢功能,从而有针对性的制定个体化超促排卵的最佳方案,以提高体外受精的成功率。通过检测窦卵泡的数量对超排卵周期中患者的卵巢反应性进行预测,不仅有助于促排卵方案的顺利实施,而且可以提高人工授精的成功率,从而减少辅助生殖治疗产生的不良后果^[20]。

综上所述,窦卵泡计数可以直观的、客观的评价患者的卵巢功能,不仅为患者的体外受精成功率起到预测的作用,而且在一定程度上能够帮助我们采取合理的正确的促排卵方案对患者进行有效治疗并预测其妊娠结局,为临床不孕不育症的治愈提供参考。

参考文献(References)

- [1] Wiser A, Gonen O, Ghetler Y, et al. Monitoring stimulated cycles during in vitro fertilization treatment with ultrasound only-preliminary results[J]. *Gynecol Endocrinol*, 2012, 28(6): 429-431
- [2] 黄彦妮, 苏亮, 谭丽娟, 等. 促排卵周期中未破裂黄素化卵泡综合征与性激素的关系探讨 [J]. *现代生物医学进展*, 2012, 12(3): 504-507+488
Huang Yan-ni, Su Liang, Tan Li-juan, et al. Analysis on the Relationship between Luteinized Unruptured Follicle Syndrome and Hormone in the Cycle of Ovulation Induction[J]. *Progress in Modern Biomedicine*, 2012, 12(3): 504-507+488
- [3] Lin H, Wang W, Li Y, et al. Triggering final oocyte maturation with reduced doses of hCG in IVF/ICSI: a prospective, randomized and controlled study[J]. *Eur J Obstet Gynecol Reprod Biol*, 2011, 159(1):

- 143-147
- [4] Guivarc'h-Levé que A, Jaffré F, Homer L, et al. GnRH agonist triggering in IVF and luteal phase support in women at risk of ovarian hyperstimulation syndrome [J]. *Gynecol Obstet Fertil*, 2013, 41(9): 511-514
- [5] Omurtag K, Cooper A, Bullock A, et al. Sperm Recovery and IVF after Testicular Sperm Extraction (TESE): Effect of Male Diagnosis and Use of Off-Site Surgical Centers on Sperm Recovery and IVF[J]. *PLoS One*, 2013, 29, 8(7): 69838
- [6] 黄仲英, 李尚为, 马黔红, 等. 移植胚胎数目对高龄不孕患者 IVF-ET 结局的影响[J]. *现代生物医学进展*, 2009, 9(5): 835-837
Huang Zhong-ying, Li Shang-wei, Ma Qian-hong, et al. The influence of transferred embryo's number on pregnancy outcomes in aged infertile patients undergoing IVF-ET [J]. *Progress in Modern Biomedicine*, 2009, 9(5): 835-837
- [7] Palomba S, Falbo A, Carrillo L, et al. Metformin reduces risk of ovarian hyperstimulation syndrome in patients with polycystic ovary syndrome during gonadotropin-stimulated in vitro fertilization cycles: a randomized, controlled trial[J]. *Fertil Steril*, 2011, 96(6): 1384-1390
- [8] 丁海珍, 于宝生. 促性腺激素抑制激素与生殖轴的关系 [J]. *现代生物医学进展*, 2010, 10(23): 4598-4600+4597
Ding Hai-zhen, Yu Bao-sheng. Relationship between Gonadotropin-Inhibitory Hormone and Hypothalamus-Pituitary-Gonadal Axis [J]. *Progress in Modern Biomedicine*, 2010, 10(23): 4598-4600+4597
- [9] 付敏, 钱卫平, 房尚华, 等. GnRH 拮抗剂在超促排卵中的应用[J]. *现代生物医学进展*, 2013, 13(21): 4117-4118+4026
Fu Min, Qian Wei-ping, Fang Shang-hua, et al. The Application of GnRH-antagonist to Mediate Ovarian Hyperstimulation [J]. *Progress in Modern Biomedicine*, 2013, 13(21): 4117-4118+4026
- [10] Chang MY, Chiang HH, Hsieh IT, et al. Use of theantral follicle count to predict the outcome of assisted reproductive technologies[J]. *Fertil Steril*, 1998, 69: 509-510
- [11] 高彦, 王峰, 冒韵东, 等. 体外受精/单精子卵胞浆内注射-胚胎移植治疗前宫腔镜手术对妊娠结局的影响 [J]. *现代生物医学进展*, 2009, 9(8): 1496-1498+1514
Gao Yan, Wang Wei, Mao Yun-dong, et al. Effect of hysteroscopy before IVF/ICSI-ET treatment on pregnancy outcome [J]. *Progress in Modern Biomedicine*, 2009, 9(8): 1496-1498+1514
- [12] Shaltout A, Shohyab A, Youssef MA. Can dopamine agonist at a low dose reduce ovarian hyperstimulation syndrome in women at risk undergoing ICSI treatment cycles? A randomized controlled study[J]. *Eur J Obstet Gynecol Reprod Biol*, 2012, 165(2): 254-258
- [13] Karimzadeh MA, Ahmadi S, Oskouian H, et al. Comparison of mild stimulation and conventional stimulation in ART outcome [J]. *Arch Gynecol Obstet*, 2010, 281(4): 741-746
- [14] 周立花, 李汶, 卢光琇. FSHR, LHR 基因突变与多态对女性生殖的影响[J]. *现代生物医学进展*, 2010, 10(1): 186-189
Zhou Li-hua, Li Wen, Lu Guang-xiu. The Influence of Gene Mutations and Polymorphism of FSHR and LHR to the Female Reproduction [J]. *Progress in Modern Biomedicine*, 2010, 10(1): 186-189

- 311-320
- [7] Pascual CY, Fernandez-Crespo J, Sanchez-Pastor S, et al. Allergy to lentils in Mediterranean pediatric patients [J]. *Journal of Allergy and Clinical Immunology*, 1999, 103(1): 154-158
- [8] Martínez San Ireneo M, Ibanez Sandin M, Fernandez-Caldas E. Hypersensitivity to members of the botanical order Fabales (legumes) [J]. *Journal of Investigational Allergology & Clinical Immunology*, 2000, 10(4): 187-199
- [9] O'Neil CE, Zhanovec M, Nicklas TA. A review of food allergy and nutritional considerations in the food-allergic adult [J]. *American Journal of Lifestyle Medicine*, 2011, 5(1): 49-62
- [10] Sanchez Monge R, Lopez Torrejón G, Pascual C, et al. Vicilin and convicilin are potential major allergens from pea [J]. *Clinical & Experimental Allergy*, 2004, 34(11): 1747-1753
- [11] Misra A, Kumar R, Mishra V, et al. Partial characterization of red gram (*Cajanus cajan* L. Millsp) polypeptides recognized by patients exhibiting rhinitis and bronchial asthma [J]. *Food and Chemical Toxicology*, 2010, 48(10): 2725-2736
- [12] Sánchez-Monge R, Pascual CY, Díaz-Perales A, et al. Isolation and characterization of relevant allergens from boiled lentils [J]. *Journal of Allergy and Clinical Immunology*, 2000, 106(5): 955-961
- [13] López-Torrejón G, Salcedo G, Martín-Esteban M, et al. Len c 1, a major allergen and vicilin from lentil seeds: protein isolation and cDNA cloning[J]. *Journal of Allergy and Clinical Immunology*, 2003, 112(6): 1208-1215
- [14] Akkerdaas J, Finkina E, Balandin S, et al. Lentil (*Lens culinaris*) lipid transfer protein Len c 3: a novel legume allergen [J]. *International Archives of Allergy and Immunology*, 2011, 157(1): 51-57
- [15] 郑义成, 华萍, 杨安树, 等. 食物中过敏原检测技术研究进展[J]. *食品科学*, 2010, 31(21): 417-420
- Zheng Yi-cheng, Hua Ping, Yang An-shu, et al. Research Advance in Detection Technologies for Allergen in Food[J]. *Food Science*, 2010, 31(21): 417-420
- [16] Pauli G, Malling H-J. Allergen-Specific Immunotherapy with Recombinant Allergens [J]. *Current Topics in Microbiology and Immunology*, 2011, 352: 43-54
- [17] 武涌, 李欣, 陈红兵, 等. 食物过敏原表位定位技术的研究进展[J]. *食品科学*, 2010, 31(23): 406-410
- Wu Yong, Li Xin, Chen Hong-bing, et al. Research Progress on the Epitope Mapping Technology for Food Allergens [J]. *Food Science*, 2010, 31(23): 406-410
- [18] Kiefer F, Arnold K, Künzli M, et al. The SWISS-MODEL Repository and associated resources [J]. *Nucleic Acids Research*, 2009, 37(suppl 1): D387-D392
- [19] Korber B, LaBute M, Yusim K. Immunoinformatics comes of age[J]. *PLoS Computational Biology*, 2006, 2(6): 484-492
- [20] Goodman RE. Practical and predictive bioinformatics methods for the identification of potentially cross-reactive protein matches [J]. *Molecular Nutrition & Food Research*, 2006, 50(7): 655-660
- [21] Larsen JE, Lund O, Nielsen M. Improved method for predicting linear B-cell epitopes[J]. *Immunome Res*, 2006, 2: 2
- [22] Saha S, Raghava GP. Prediction of continuous B-cell epitopes in an antigen using recurrent neural network [J]. *Proteins*, 2006, 65 (1): 40-48

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- [15] Papanikolaou EG, Verpoest W, Fatemi H, et al. A novel method of luteal supplementation with recombinant luteinizing hormone when a gonadotropin-releasing hormone agonist is used instead of human chorionic gonadotropin for ovulation triggering: a randomized prospective proof of concept study [J]. *Fertil Steril*, 2011, 1, 95(3): 1174-1177
- [16] 郑利平, 朱旭, 覃海燕, 等. 不育男性患者和健康男性血液与精浆中微量元素含量的对比分析 [J]. *现代生物医学进展*, 2012, 12(4): 681-683
- Zheng Li-ping, Zhu Xu, Qin Hai-yan, et al. The Comparative Analysis of Trace Elements in Blood and Seminal Plasma of Infertile and Healthy Male [J]. *Progress in Modern Biomedicine*, 2012, 12(4): 681-683
- [17] Caserta D, Lisi F, Marci R, et al. Does supplementation with recombinant luteinizing hormone prevent ovarian hyperstimulation syndrome in down regulated patients undergoing recombinant follicle stimulating hormone multiple follicular stimulation for IVF/ET and reduces cancellation rate for high risk of hyperstimulation? [J]. *Gynecol Endocrinol*, 2011, 27(11): 862-866
- [18] Durmusoglu F, Elter K, Yoruk P, et al. Combining cycle day 7 follicle count with the basal antral follicle count improves the prediction of ovarian response [J]. *Fertil Steril*, 2004, 81 (4): 1073-1078
- [19] Bancsi LF, Broekmans F, Eijkemans MJ, et al. Predictor of poor ovarian response in vitro fertilization: a prospective study comparing basal markers of ovarian reserve[J]. *Fertil Steril*, 2002, 77: 328-333
- [20] Gerli S, Di Renzo GC. Establishing a combined stimulation protocol hFSH followed by rFSH might represent a breakthrough in the IVF practice[J]. *Eur Rev Med Pharmacol Sci*, 2013, 17(15): 2091-2096