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基础卵泡刺激素水平对 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: 基础卵泡刺激素(bFSH)可以刺激精子生成和促进卵子成熟,是人体内重要的激素之一。本研究针对体外受精(IVF)周期 bFSH 水平的变化情况,探讨 bFSH 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-2012 年 12 月在我院生殖医学中心接受体外受精-胚胎移植(IVF-ET)治疗的 154 例患者的临床资料,根据基础卵泡刺激素水平分为 A 组(bFSH $\geq$ 10 IU/L)、B 组($8 \leq$ bFSH $\leq$ 10 IU/L)和 C 组(bFSH $<$ 8 IU/L)。对比分析三组对象的年龄、基础窦卵泡数(bAFC)、黄体生成素(LH)含量、FSH/LH 值、促性腺激素(Gn)的用量、使用时间、受精率及临床妊娠率等。**结果:** 三组患者的年龄、bAFC 及 FSH/LH 相比较,差异具有统计学意义($P < 0.05$);三组的 Gn 用量和时间、获卵数及妊娠率比较,差异显著且具有统计学意义($P < 0.05$);三组基础 LH 值及超排卵周期受精率无显著差异($P > 0.05$)。**结论:** 基础卵泡刺激素(bFSH)对体外受精女性的卵巢储备功能具有一定的预测价值,bFSH 水平的高低可作为预测女性不孕患者超排卵周期卵巢反应性的一项重要指标,值得临床推广和应用。

关键词: 卵泡刺激素;体外受精;卵巢反应;促排卵

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

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ABSTRACT Objective: The basic follicle-stimulating hormone(bFSH) is one of the most important hormones in human body which could stimulate the production and maturity of sperm. This study aims to exploring the predictive value for ovarian response by means of observing the changes of bFSH 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 154 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 bFSH levels, the selected patients were divided into three groups, namely, the group A (bFSH $\geq$ 10 IU/L); group B ($8 \leq$ bFSH $\leq$ 10 IU/L) and group C (bFSH $<$ 8 IU/L). Then the age, the bAFC values, the time and dose of Gn, the rate of fertilization and pregnancy in three groups were compared and evaluated. **Results:** There were statistically significant differences about the age, the bAFC values, the rate of FSH and LH, the time and dose of Gn, the numbers of ovum and the rate of pregnancy ($P < 0.05$). But there was no statistically significant difference about the values of LH and the rate of fertilization in three groups ($P > 0.05$). **Conclusions:** It is indicated that the values of bFSH could predict the functions of women's ovary for those who were taken the *in vitro* fertilization and the levels of bFSH might become an essential item in the future for the clinical to detect the ovarian reactions of the infertile females during the super ovulation cycles.

Key words: Follicle-stimulating hormone; *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治疗中并取得了一定的效果。体外受精的成功率受多重因素的影响,若女性不孕患者的卵巢反应性差就会导致超排卵周期中排卵过少

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甚至不排卵的现象发生,严重影响 IVF-ET 的成功率^[1-3]。那么如何精确的评价卵巢的储备功能、针对不同的患者制定最佳的促排卵方案是目前临床生殖医学领域关注的热点问题。基础卵泡刺激素(bFSH)作为人体内重要的激素,作用于女性的卵巢可以促进卵泡颗粒层细胞的生殖和分化,促进卵子成熟。卵泡刺激素与卵巢排卵关系密切,基础卵泡刺激素的水平变化可反映卵巢的分泌功能^[4-6]。有研究证实,bFSH 水平随着患者年龄的增加而升高,说明其对卵巢储备功能的预测更敏感^[7]。我们通过研究 bFSH 对 IVF/ICSI-ET 超排卵周期卵巢反应的预测价值,力求科学全面的分析卵巢的储备功能,从而制定最佳治疗方案,为提高 IVF-ICSI-ET 的临床妊娠率提供参考。

1 资料与方法

1.1 研究对象

选取 2012 年 1 月 - 2012 年 12 月在我院生殖医学中心接受 IVF/ICSI-ET 的患者 154 例。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;不孕期限为 1-12 年,平均 5.08 ± 2.91 年。不孕的原因:女性输卵管因素,如子宫内膜异位症、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 FSH 值,将所选病例分为三组,A 组:29 例,bFSH ≥ 10 IU/L;B 组:37 例, $8 \text{ IU/L} \leq \text{bFSH} \leq 10 \text{ IU/L}$;C 组:88 例,bFSH $< 8 \text{ IU/L}$ 。

1.2 方法

1.2.1 激素水平测定 分别于排卵周期前一经期的第二天及排卵后的第 13-15 天抽取患者静脉血。采用免疫化学发光法测定患者血清中的基础卵泡刺激素(bFSH)、LH、T、E₂、垂体泌乳素(PRL)、人绒毛膜促性腺激素(hCG)等^[8]。放射免疫分析药盒由北京北方生物技术研究所提供,组间变异及组内变异均 $< 5\%$ 。

1.2.2 促排卵方案 患者月经来潮后的 2-5 天行 B 超检查窦卵

泡数以排除卵巢囊肿;促排卵采用重组人促卵泡激素(r-FSH, 75-150 IU, 5.5 $\mu\text{g}/75 \text{ IU}$, 生产批号: S20080030);根据卵泡发育情况调整用药剂量,当直径达 18 mm 的卵泡数超过两个时应采取皮下注射 10000 IU HCG;于第 34-36 经阴道 B 超行穿刺取卵^[9]。

1.2.3 IVF-ET 常规行体外受精,18 小时后观察原核和极体等评价受精情况,第二、第三天观察胚胎情况;第三天细胞数达 6-10 个、卵裂球形态规则且碎片 $\leq 15\%$ 的视为优质胚胎;胚胎移植后的 14 天,检测患者血常规及 hCG;第 28-35 天经 B 超检查可见孕囊、胚芽及原始心管搏动或手术病检证实为异位妊娠者均诊断为临床妊娠^[10]。

1.3 观察指标

观察三组患者的年龄、基础卵泡刺激素 (bFSH)、窦卵泡 (AFC)、促黄体生成素 (LH)、卵泡刺激素与黄体生成素比值 (FSH/LH)、促性腺激素(Gn)的用量及使用时间、获卵数、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,计量资料采用方差分析,计数资料以百分率表示并用 χ^2 检验,结果以均数 $\pm$ 标准差 ($\bar{X} \pm S$) 表示,以 $P < 0.05$ 为差异具有统计学意义。

2 结果

2.1 三组患者的基本资料

如表 1 所示,A 组平均年龄为 (35.38 ± 5.47) 岁;bAFC 为 (5.31 ± 3.54) IU/L;LH 为 (4.87 ± 1.70);FSH/LH 为 (3.09 ± 1.32)。B 组平均年龄为 (33.41 ± 5.56) 岁;bAFC 为 (12.65 ± 11.56) IU/L;LH 为 (4.14 ± 1.94);FSH/LH 为 (2.79 ± 1.82)。C 组平均年龄为 (31.67 ± 4.40) 岁;bAFC 为 (15.28 ± 15.45) IU/L;LH 为 (4.17 ± 2.85);FSH/LH 为 (2.09 ± 1.12)。三组患者的基础 LH 值比较,无显著差异 ($P > 0.05$);年龄、bAFC 及 FSH/LH 比较差异明显,具有统计学意义 ($P < 0.05$)。

表 1 三组临床资料

Table 1 Clinical data of patients in three groups

Group	Cycle(case)	Age(year)	bAFC	LH	FSH/LH
A($\geq 10 \text{ IU/L}$)	29	35.38 ± 5.47	5.31 ± 3.54	4.87 ± 1.70	3.09 ± 1.32
B($8-10 \text{ IU/L}$)	37	33.41 ± 5.56	12.65 ± 11.56	4.14 ± 1.94	2.79 ± 1.82
C($< 8 \text{ IU/L}$)	88	31.67 ± 4.40	15.28 ± 15.45	4.17 ± 2.85	2.09 ± 1.12

2.2 三组超排卵周期的卵巢反应情况

如表 2 所示,A 组 Gn 用量为 (43.9 ± 19.5) IU;使用时间为 (10.17 ± 3.81) 天;获卵数为 (8.10 ± 5.35) 个;受精率为 84%;临床

妊娠率为 20%。B 组 Gn 用量为 (33.86 ± 13.96) IU;使用时间为 (10.92 ± 4.14) 天;获卵数为 (12.51 ± 8.71) 个;受精率为 85%;临床妊娠率为 32%。C 组 Gn 用量为 (33.40 ± 12.37) IU;使用时间为 (11.11 ± 4.78) 天;获卵数为 (18.15 ± 11.27) 个;受精率为 88%;

表 2 三组患者基础 FSH 及超排卵周期卵巢反应

Table 2 Values of bFSH and reactions of the ovary in three groups

Group	Gn level(IU)	Time(day)	Ovum	Fertilization(%)	Pregnancy(%)
A($\geq 10 \text{ IU/L}$)	43.90 ± 19.50	10.17 ± 3.81	8.10 ± 5.35	84	20
B($8-10 \text{ IU/L}$)	33.86 ± 13.96	10.92 ± 4.14	12.51 ± 8.71	85	32
C($< 8 \text{ IU/L}$)	33.40 ± 12.3	11.11 ± 4.78	118.15 ± 11.27	88	47
P	0.001	> 0.05	0.000	> 0.05	< 0.05

临床妊娠率为 47%。由此可知, A 组 Gn 用量最多, 但获卵数最少、妊娠率最低; C 组 Gn 用量最少、使用时间最长, 但获卵数最多、妊娠率最高, 差异具有统计学意义($P < 0.05$)。

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。bFSH 值、抑制素 B、AMH 及超声检查等是临床上常用的评估卵巢储备功能的指标^[11,12]。Muasher 等^[14]在 1988 年首次提出了 bFSH 水平对 IVF 周期卵巢反应性具有预测作用, 而且与 IVF 的临床妊娠率成负相关。相关研究显示, bFSH 水平高的年轻女性行 IVF 周期的取消率高, 但对症处理后仍会获得理想的妊娠率, bFSH 水平的高低与年龄小于 35 岁的不孕症患者的活婴出生率无明显相关性^[18,19]。另有研究指出, 随着患者年龄的增长或 bFSH 水平的升高, 其获卵数、受精率及可移植胚胎数均不同程度的下降。因此, 将年龄与 bFSH 水平相结合用于预测卵巢反应性将获得更好的效果^[15]。据相关文献报道, 随着 FSH 值的升高, 卵泡的发育及卵子的质量降低, 促排卵后卵巢的反应性也随之变差, 因而将患者的年龄与窦卵泡数结合对卵巢储备及 IVF 妊娠结局的预测效果更好^[16]。结合本研究, 我们采用 Gn 促排卵, 分析 bFSH 与各种指标的相关性, 结果发现 bFSH 值与卵泡个数、Gn 用量、临床妊娠率呈负相关, 说明 bFSH 越高, 用药后卵泡个数越少, 妊娠率越低。此外, 我们还发现随着女性年龄的增长, 其卵巢反应性及卵母细胞质量都有所下降, 必然影响妊娠结局。bFSH 的测定方法简单, 但也存在一定局限性, 如基础 E2 水平的升高会通过负反馈抑制 bFSH 值, 影响 bFSH 对卵巢功能的判断^[13,17]。由于基础 FSH 存在很大的周期性差异, 我们需要进行多次检验、重复化验结果并且排除药物干扰才能获得较稳定的真实的 bFSH 值。既往研究表明, 若综合多个指标对卵巢功能进行测定, 可获得更好的效果, 如利用 FSH 与 LH 的比值判断卵巢储备功能, 并加以合理的用药和个性化的促排卵方案, 以利于提高妊娠率, 特别是 bFSH 水平偏高患者的妊娠率^[20]。

综上所述, 本研究表明基础 FSH 值可以预测 IVF/ICSI 卵巢的反应性, 从而制定最佳的刺激方案, 加强卵巢反应的敏感度, 提高体外受精的成功率。因此, bFSH 的水平变化情况可作为评估卵巢功能的重要指标之一, 值得临床推广。

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