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## 维生素 D 在多囊卵巢综合征患者中的表达

桂娟 张婕 徐望明 谢青贞 夏旂

**摘要** 目的 评估辅助生殖技术中多囊卵巢综合征(PCOS)患者血清中维生素D水平及其与胚胎质量和妊娠率之间的关系。**方法** 本研究共纳入了辅助生殖助孕治疗中的32例PCOS患者和因输卵管因素导致不孕的28例对照。检测血清中25羟维生素D水平,记录体重指数、获卵数、受精率、优胚率和妊娠率用于分析。**结果** 两组均有较高的维生素D缺乏率。与对照组比较,血清维生素D水平在PCOS组( $P=0.041$ )显著降低。但两组间优胚率和妊娠率比较,差异均无统计学意义。维生素D缺乏与否与上述指标也没有相关性。**结论** 维生素D缺乏在不孕症人群中普遍存在,PCOS妇女尤甚。但是尚未发现维生素D缺乏与胚胎质量与妊娠率之间的关系,仍需要开展大样本数据深入研究探讨。

**关键词** 维生素D 多囊卵巢综合征 辅助生殖技术

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**Serum Vitamin D Status in Women with Polycystic Ovary Syndrome.** Gui Juan, Zhang Jie, Xu Wangming, *et al.* Renmin Hospital of Wuhan University, Hubei 430060, China

**Abstract Objective** To assess the serum vitamin D level in polycystic ovary syndrome (PCOS) referred for assisted reproductive technology (ART) and relationship between the serum vitamin D status and the quality of the embryos and pregnant rate in these women.

**Methods** Thirty-two women with PCOS and 28 control women with tubal infertility referred for ART were recruited. Serum levels of 25 (OH) vitamin D was measured. The body mass index, fertilization rate, high-quality embryo rate, biochemical pregnant rate and clinical

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cal pregnant rate were documented for analysis. **Results** The incidence of vitamin D deficiency were both high in these two groups. When compared with control, the serum vitamin D level was significantly decreased in PCOS group ( $P=0.041$ ). There was no significant difference in high-quality embryo rate and pregnant rate between the two groups. Vitamin D deficiency had no relation with the high-quality embryo rate and pregnant rate. **Conclusion** Vitamin D deficiency is common in the population of IVF, especially in those PCOS women. However, the effects of vitamin D on the quality of the embryos and pregnant rate are not found. Appropriately designed studies are needed to better explore the influence of vitamin D in PCOS and ART patients.

**Key words** Vitamin D; Polycystic ovary syndrome; Assisted reproductive technology

维生素D是一种类固醇类激素,主要是通过皮肤暴露于阳光下由17羟基胆固醇内源性合成产生,10%~20%由肠道吸收而来。近年来,研究显示维生素D在女性生殖领域中有重要作用。对多囊卵巢综合征(polycystic ovarian syndrome, PCOS)、子宫内膜异位症、子宫肌瘤、卵巢早衰和体外受精技术等均有相关影响<sup>[1]</sup>。

多囊卵巢综合征是育龄女性最常见的生殖内分泌疾病,可伴有胰岛素抵抗、高胰岛素血症和血脂异常等表现。有研究显示PCOS患者中普遍存在维生素D缺乏情况,比率高达67%~85%<sup>[2-6]</sup>。维生素D缺乏可能与PCOS的临床表现和代谢障碍相关,如胰岛素抵抗、血脂异常、肥胖和糖耐量异常等<sup>[7,8]</sup>。还有研究显示即使是正常体重的PCOS患者的维生素D水平仍低于正常对照人群<sup>[9]</sup>。这些都提示维生素D可能参与PCOS的病理生理变化。

与此同时,一些给予维生素D补充的治疗性实验结果提示,给予维生素D缺乏的PCOS患者补充维生素D后,可改善血压,降低血清抗苗勒管激素水平,减轻胰岛素抵抗、总睾酮水平和雄烯二酮水平<sup>[10-12]</sup>。然而,一篇关于维生素D补充实验的Meta分析提示,补充维生素D仅能降低总睾酮水平<sup>[13]</sup>。而另一篇Meta分析结果显示,补充维生素D可以降低PCOS妇女的甘油三酯,但对胰岛素代谢和雄激素水平没有影响<sup>[14]</sup>。还有一些Meta分析甚至没有发现补充维生素D对改善PCOS患者的代谢和性激素异常有任何意义<sup>[15-19]</sup>。

鉴于既往研究结果的不均一性,维生素D在辅助生殖助孕治疗中的PCOS患者中是否存在缺乏仍有待研究,并且维生素D与PCOS患者胚胎质量和妊娠率的关系也尚不清楚。因此本研究旨在评估辅助生殖助孕治疗中的PCOS患者和对照人群的血清维生素D水平及其与受精率、优质胚胎率和妊娠率之间的关系。

## 材料与方法

1. 研究对象:本研究共纳入60例于2017年6

月~2018年6月在武汉大学人民医院生殖医学中心行辅助生殖助孕治疗的患者,其中PCOS患者32例,因输卵管因素导致不孕的对照人群28例。所有研究对象年龄为21~38岁。本研究经武汉大学人民医院伦理学委员会的批准,每位研究对象均签署了知情同意书,严格遵守赫尔辛基宣言。本研究中所有研究对象获卵数均在15枚以上。PCOS患者的纳入标准为至少满足以下3条中的2条:①稀发排卵或无排卵;②高雄激素临床表现或实验室检查雄激素水平增高;③超声提示双侧卵巢中2~8mm卵泡数目多于12个。排除标准:患者有其他内分泌疾病或其他引起雄激素增高的疾病如分泌雄激素的肿瘤,先天性肾上腺皮质增生症和库欣综合征;有内科疾病患者(如高血压、糖尿病、肝脏疾病、甲状腺功能异常等);有肿瘤病史患者;合并男方少弱精症。对照组排除标准同PCOS组。

2. 收集资料:所有纳入者,在采卵后采集空腹静脉血进行血清标本检测维生素D水平。维生素D浓度测定均由武汉大学人民医院医学检验中心依据相应的试剂说明书进行检测。维生素D水平分类的标准为:25-羟基维生素D<10ng/ml(25nmol/L)为严重缺乏;25-羟基维生素D在10~20ng/ml(25~50nmol/L)为缺乏;25-羟基维生素D在21~29ng/ml(51~74nmol/L)为不足;25-羟基维生素D>30ng/ml(75nmol/L)为充足<sup>[20]</sup>。收集纳入者的年龄、体重指数、获卵数、受精率、优质胚胎率,随访生化妊娠率和临床妊娠率等资料。

3. 统计学方法:采用SPSS 19.0统计学软件对数据进行统计分析,计数资料用频率或百分比表示,组间差异比较采用 $\chi^2$ 检验或Fisher's精确检验。计量资料首先进行正态分布检验,若为正态分布,则用均值±标准差( $\bar{x} \pm s$ )表示;若为非正态分布,则用中位数(四分位间距)表示。然后根据实际需要采用两个独立样本T检验或非参数秩和检验来判断组间差异,以 $P<0.05$ 为差异有统计学意义。

## 结 果

两组间年龄、体重指数、获卵数、受精率、优胚率、

生化妊娠率和临床妊娠率之间比较,差异均无统计学意义(表1)。两组患者均存在维生素D缺乏,根据维生素D水平分类,PCOS组50%为维生素D缺乏,25%为严重缺乏,21.9%为不足,3.1%为充足。对照组32.1%为维生素D缺乏,14.3%为严重缺乏,50%为不足,3.6%为充足。PCOS组维生素D缺乏率(缺乏加重严重缺乏)为75%,对照组的缺乏率为46.4%。与对照组相比,PCOS组的维生素D缺乏率显著升高( $P=0.023$ )。血清维生素D水平在PCOS组显著降低( $P=0.041$ )。进行相关性分析时,未发现维生素D缺乏与各组的体重指数、获卵数、受精率、优胚率、生化妊娠率和临床妊娠率之间有相关性。

表1 多囊卵巢综合征患者和对照人群的  
临床信息比较 ( $\bar{x} \pm s$ )

| 项目                       | 对照组<br>( $n=28$ ) | 多囊卵巢综合征组<br>( $n=32$ ) | $P$   |
|--------------------------|-------------------|------------------------|-------|
| 年龄(岁)                    | 29.89 $\pm$ 3.00  | 28.53 $\pm$ 3.35       | 0.110 |
| 体重指数(kg/m <sup>2</sup> ) | 21.94 $\pm$ 2.48  | 23.16 $\pm$ 3.14       | 0.100 |
| 维生素D水平(ng/ml)            | 19.70 $\pm$ 7.42  | 15.98 $\pm$ 6.38       | 0.041 |
| 获卵数(个)                   | 22.68 $\pm$ 4.02  | 24.25 $\pm$ 5.31       | 0.210 |
| 受精率(%)                   | 50 $\pm$ 21       | 49 $\pm$ 19            | 0.820 |
| 优胚率(%)                   | 71 $\pm$ 26       | 59 $\pm$ 33            | 0.110 |
| 生化妊娠率(%)                 | 67.9              | 79.3                   | 0.330 |
| 临床妊娠率(%)                 | 60.7              | 62.1                   | 0.920 |

PCOS组的促排卵方案构成比与对照组比较差异有统计学意义( $P=0.001$ )。PCOS组主要采用超长方案(43.8%)和拮抗剂方案(31.3%)促排卵,对照组主要采用常规长方案(60.7%)促排卵。但按照促排卵方案分亚组后,常规长方案、超长方案和拮抗剂方案中的PCOS患者和对照人群的年龄、体重指数、获卵数、受精率、优胚率、生化妊娠率和临床妊娠率之间比较,差异均无统计学意义。

## 讨 论

研究表明维生素D在PCOS的发生、发展中起了一定的作用。它可以增强胰岛素的合成和释放,增加胰岛素受体的表达同时抑制加重胰岛素抵抗的炎症细胞因子的表达<sup>[21]</sup>。本研究中纳入的PCOS患者体重指数平均值在正常范围,因为在进入周期前PCOS患者基本都有预处理,如减重、降低雄激素或血脂血糖等治疗,但结果仍显示辅助生殖助孕治疗中的PCOS患者的血清维生素D水平显著低于对照组,即便这些PCOS患者经过了减重、降雄或者减轻胰岛素抵抗的相关治疗。这提示维生素D参与PCOS的病

理生理改变,与其发病类型不具有相关性,具体机制还有待于进一步探讨。但是,本研究并未发现维生素D与受精率、优胚率、妊娠率之间的关系,考虑可能为血清中的维生素D不能完全反映卵巢和子宫内膜局部的水平,而局部的维生素D水平可能更能体现其与胚胎质量和妊娠率之间的关系。

本研究结果显示在PCOS组的维生素D缺乏率高达75%,这与英国的一项研究报道的发生率较一致(72%)<sup>[5]</sup>。然而,在一项澳大利亚的PCOS患者的研究中提示其维生素D缺乏率为38.8%,严重缺乏率仅为2.9%<sup>[4]</sup>。考虑各地的气候、饮食和文化习惯可能是导致发生率的巨大差异的原因。因为中国女性喜欢遮阳防晒,而英国的阴雨天气较多,冬令时期日照时间短,检测维生素D的试剂盒及检测方法不同,这些都有可能造成巨大的差异。此外,本研究还发现对照组人群维生素D缺乏的比率也很高(51.2%),说明维生素D缺乏在辅助生殖助孕治疗的患者中普遍存在。这种高比率的维生素D缺乏也给公共卫生系统发出了警告,可能需要改变生活方式进行早期干预。

为了减少各种促排卵方案对结果的影响,笔者选择了获卵数为15个以上的患者进行研究,排除了男方因素对受精率和胚胎质量的影响。血清维生素D均在采卵后采集静脉血做检测。在采卵的节点检测更能反映其与卵子质量和妊娠率的关系。因为有些患者在启动IVF周期后有可能服用复合维生素片,如爱乐维或善纯等,其中都含有少量的维生素D。使得启动初期的维生素D水平不能代表最终的维生素D水平。当然本研究也存在一些不足之处:如样本量太小,所有PCOS患者进入试管周期前均有预处理如减重,所以无法判断体重与维生素D缺乏之间的关系。而且,本研究只检测了血清中的维生素D水平,可能不能完全反映维生素D对胚胎质量和子宫内膜容受性的作用。所有需要进一步的研究来探讨维生素D在子宫和卵巢局部的作用以及给予维生素D补充实验来观察其治疗效应。

总之,维生素D缺乏在不孕症人群中普遍存在,PCOS患者较对照人群更为严重。但是尚未发现维生素D缺乏与胚胎质量与妊娠率之间的关系,需要进一步开展大样本的数据分析探讨维生素D在PCOS和不孕症人群中的作用。

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