

网络出版时间:2026-03-18 09:26:26 网络出版地址:https://link.cnki.net/urlid/34.1065.R.20260317.1544.004

高孕激素促排卵方案对不孕症患者胚胎整倍体率及临床妊娠结局的影响分析

王敏捷¹,张永静¹,钱锦¹,王超^{1,2,3},徐玉萍^{1,2,3},王田娟^{1,2,3},陈大蔚^{1,4,5},郝燕^{1,4,5},邢琼^{1,2,3}

(¹安徽医科大学第一附属医院妇产科,合肥 230022;²国家卫生健康委配子及生殖道异常研究

重点实验室,合肥 230022;³安徽医科大学出生人口健康教育部重点实验室,合肥 230032;

⁴安徽省生命资源保存与人工器官教育部工程研究中心,合肥 230032;

⁵生殖健康与遗传安徽省重点实验室,合肥 230032)

摘要 **目的** 分析高孕激素(PPOS)方案对不孕症患者胚胎整倍体率及临床妊娠结局的影响。**方法** 选取进行胚胎植入前非整倍体遗传学检测(PGT-A)周期的女性为研究对象(共656个周期、3 081个囊胚),根据年龄和促排卵方案分为≤35岁组与>35岁组[PPOS组($n=48,60$),黄体期长方案(LP)组($n=160,57$),拮抗剂方案(AP)组($n=220,111$)]。分别比较不同年龄组中3组促排方案的一般情况、卵巢刺激情况、胚胎情况,并比较3组促排方案首次冻融胚胎移植(FET)的妊娠结局,其中主要观察指标为胚胎整倍体率。**结果** ①≤35岁组中,PPOS组基础卵泡刺激素(bFSH)高于LP组和AP组,基础卵泡刺激素/基础黄体生成素(bFSH/bLH)高于AP组($P<0.05$),年龄>35岁组中,PPOS组和AP组的bFSH水平高于LP组($P<0.05$)。②≤35岁组:PPOS组与LP组、AP组在成熟卵子率(MII卵率)、双原核受精率(2PN)受精率、卵裂率、2PN卵裂率、囊胚形成率、优质胚胎率及整倍体率差异均无统计学意义,但PPOS组的获卵总数、MII卵数、2PN受精数、卵裂数、2PN卵裂数、囊胚形成数、优质胚胎数、高评分囊胚数、可移植胚胎数、冷冻胚胎数、囊胚检测数、整倍体数、至少有一个整倍体率小于其他2组;>35岁组:PPOS组与LP组、AP组在MII卵率、2PN卵裂率、囊胚形成率、整倍体数、整倍体率、至少一个整倍体率差异均无统计学意义,但PPOS组的获卵总数、MII卵数、2PN受精数、卵裂数、2PN卵裂数、囊胚形成数、可移植胚胎数、冷冻胚胎数小于LP组($P<0.05$);优质胚胎率小于AP组($P<0.05$);优质胚胎数、高评分囊胚数、囊胚检测数小于其他2组($P<0.05$);2PN受精率高于AP组;卵裂率高于其他2组($P<0.05$)。③3组首次FET的生化妊娠率、临床妊娠率、活产率、早期流产率及晚期流产率差异无统计学意义。**结论** PPOS方案相较其他两种方案对胚胎整倍体率及临床妊娠率无显著影响。然而,在行PGT-A的全胚冷冻周期中,PPOS方案并不降低胚胎染色体的正常率,但会减少可用的胚胎总数,可能不适合年轻女性,但对于高龄女性而言,PPOS方案可作为促排卵方案的一种选择。

关键词 高孕激素方案;黄体期长方案;拮抗剂方案;胚胎整倍体率;冻融胚胎移植

中图分类号 R 711.6

文献标志码 A **文章编号** 1000-1492(2026)05-0923-09

doi:10.19405/j.cnki.issn1000-1492.2026.05.017

随着辅助生殖技术的快速发展,促排卵方案的个体化选择对体外受精-胚胎移植(*in vitro* fertilization and embryo transfer, IVF-ET)结局具有决定性影响。胚胎非整倍体是移植失败的重要原因,高龄、反复种植失败等情况是进行胚胎植入前非整倍体遗传学检测(preimplantation genetic testing for aneuploidy, PGT-A)的明确指征^[1]。高龄女性胚胎整倍

体率显著降低,且随年龄增长而下降^[2]。高孕激素促排卵(progesterin primed ovarian stimulation, PPOS)方案利用孕激素抑制早发黄体生成素(luteinizing hormone, LH)峰,在卵巢低反应患者中展现出独特价值,可降低卵巢过度刺激综合征(ovarian hyperstimulation syndrome, OHSS)风险并优化卵泡发育^[3-4]。然而,PPOS对胚胎整倍体率的影响目前研究结论不一^[5-6],部分研究提示高龄患者使用PPOS后整倍体率可能降低,而近期高质量随机对照试验和荟萃分析显示在全年龄段人群中PPOS方案和拮抗剂方案(gonadotropin-releasing hormone antagonist protocol, AP)相比,其整倍体率无显著差异,这种差

2026-02-06 接收

基金项目:安徽省转化医学研究院科研基金项目(编号:2023zhxy-C38)

作者简介:王敏捷,女,硕士研究生;

邢琼,女,副教授,主任医师,硕士生导师,通信作者, E-mail: joan2004207@163.com

异可能与研究设计和人群分层有关。为此,该研究旨在回顾性分析不同促排卵方案(特别是PPOS)在不同年龄分组中对胚胎整倍体率的影响,以期为临床促排卵策略的选择提供科学依据。

1 材料与方法

1.1 研究对象与分组 本研究采用回顾性队列研究,选取2021年1月—2024年6月在安徽医科大学第一附属医院生殖中心行PGT-A助孕的331例患者为研究对象,共纳入656个促排卵周期、3 081个囊胚,根据年龄及促排卵方案 ≤ 35 岁组与 >35 岁组[PPOS组($n=48、60$),黄体期长方案(gonadotropin-releasing hormone antagonist protocol, LP)组($n=160、57$),AP组($n=220、111$)]。纳入标准:因高龄、复发性流产或反复种植失败行PGT-A周期助孕。排除标准:①夫妇一方或双方染色体结构性异常或单基因病;②女方合并有内科系统类或代谢类疾病,如肝炎急性期、甲状腺功能亢进、急性肾炎或慢性肾功能不全等;③临床资料不全或失访者。所有患者均签署知情同意书。本研究通过安徽医科大学第一附属医院伦理委员会批准(伦理号:PJ2025-10-94)。

1.2 方法

1.2.1 PPOS方案 月经第2~3天开始口服醋酸甲羟孕酮(medroxyprogesterone, MPA)4~10 mg,同时给予促性腺激素(gonadotropin, Gn)150~300 IU/d进行促排,常规通过B超及血清黄体生成素、雌二醇(estradiol, E_2)、孕酮(progesterone, P)监测卵泡发育,根据卵泡生长速度调整促排药物剂量。阴道彩超(transvaginal ultra-sound, TVS)检测到有1个优势卵泡直径达到18 mm(或2个卵泡直径 ≥ 17 mm)时,予以人绒毛膜促性腺激素(human chorionic gonadotropin, HCG)10 000 IU促进卵泡成熟(扳机)^[7],36~38 h后在TVS引导下取卵。根据胚胎检测结果,再做内膜准备。

1.2.2 LP组 前次月经的第18~22天开始使用长效促性腺激素释放激素(gonadotropin-releasing hormone, GnRH)激动剂1/4~1/3剂量使垂体降调节;当垂体抑制达到适当水平:血清LH < 5 IU/L, $E_2 < 50$ ng/L,子宫内膜厚度 < 5 mm,无功能性卵巢囊肿时,开始给予外源性Gn,持续时间为8~12 d左右。促排卵过程监测、扳机时机的决定及取卵同高孕激素方案。

1.2.3 AP组 月经第2~3天开始使用Gn促排卵,于用药后第6天或优势卵泡达到12 mm同时结合激素水平开始灵活使用GnRH拮抗剂至扳机,根据超声及血清激素水平判断卵巢对药物的反应性并调整促排卵药物的使用剂量。促排卵过程监测、扳机时机的决定及取卵同高孕激素方案。

1.2.4 胚胎培养 取卵后对所有成熟的卵母细胞(metaphase II, MII)行卵胞浆内单精子注射(intracytoplasmic sperm injection, ICSI),再转入胚胎培养液中培养^[7],胚胎在辅助孵化下培养到囊胚期,第5~6天根据Gardner评分标准评估囊胚的形态特征,再进行胚胎活检,然后冻存。活检胚胎需满足以下条件:①根据囊胚的发育和孵化情况,分为3期及以上的囊胚;②囊胚内细胞团(inner cell mass, ICM)分级为C级及以上。

1.2.5 胚胎检测 根据患者要求对全部或部分达标囊胚进行检测,用固定针将内细胞团固定在9点方向处,在透明带的3点方向处激光打孔,用直径30 μ m的活检针从透明带开口处吸取5~10个滋养外胚层细胞活检,活检后的囊胚编号并立即冷冻,再运用高通量测序(next generation sequencing, NGS)从处理后的细胞中提取并纯化部分遗传物质,共计对3 081个囊胚进行了NGS测序。整个过程必须避免外源性DNA污染。囊胚活检后尽快行玻璃化冷冻方法单个囊胚保存。使用REPLI-g单细胞试剂盒进行全基因组扩增,在DNA片段化和序列文库构建完成后,使用Miseq NGS系统平台(Illumina)进行平行测序和比对,并通过BlueFuse Multi Software V4.4(Illumina)进行生物信息学分析。为确保结果的准确性,最终诊断由3名熟练技术人员根据厂商协议分别验证。最后依据获得的报告结果选择整倍体胚胎进行单胚胎解冻移植^[7]。

1.2.6 内膜准备 取卵后,如胚胎检测有可移植胚胎,再开始内膜准备,依据患者月经周期情况,选用的内膜准备方案为自然周期和替代周期方案。月经周期规律,正常排卵的患者优先选择自然周期方案,在B超监测提示排卵后,加用黄体支持(口服地屈孕酮20~40 mg/d),5 d后移植。排卵障碍或子宫内膜发育不良的患者可选择激素替代周期,月经周期的第2~3天给予戊酸雌二醇片4~6 mg,TVS监测内膜厚度达到至少8 mm且均匀,再给予地屈孕酮口服(20~40 mg/d)或黄体酮针剂注射(60 mg/d)转化

内膜,5 d后移植。

1.2.7 妊娠判定 移植后继续黄体支持至移植后14 d行血HCG监测是否妊娠,30 d后行TVS检查宫腔内是否有孕囊及心管搏动确定是否临床妊娠。

1.2.8 观察指标 ① 年龄、不孕年限、体质量指数(body mass index, BMI)、基础卵泡刺激素(follicle stimulating hormone, FSH)、LH、E₂、P(bFSH、bLH、bE₂、bP)。② 促排卵结局:Gn总量、Gn天数、HCG日LH、HCG日E₂、HCG日P。③ 实验室结局:获卵数、MII卵数、MII卵率、双原核受精(two pronucleus, 2PN)数、2PN受精率、卵裂数、卵裂率、2PN卵裂数、2PN卵裂率、囊胚形成数、优胚数、优胚率、囊胚检测数、整倍体率、至少一个整倍体率^[7-8](至少一个整倍体率=至少有一个整倍体的人数/总人数×100%)。④ 首次胚胎移植结局:生化妊娠率、临床妊娠率、早期流产率、晚期流产率、活产率。鉴于行首次胚胎移植的患者有限,为保持足够的统计效力,首次胚胎移植结局的分析将在总体样本中进行,不进行年龄亚组划分。

1.3 统计学处理 采用SPSS 26.0软件进行统计分析,所有计量资料均不符合正态分布,以M(P₂₅, P₇₅)表示,采用Kruskal-Wallis检验(H检验)。所有计数资料用n(%)表示,用χ²检验或Fisher确切概率法。与评估指标间的关联性因素分析采用多元Logistic回归,评估指标为比值比(odds ratio, OR)及95%置信区间(95% confidence interval, 95%CI)。P

<0.05为差异有统计学意义。

2 结果

2.1 3组患者一般资料比较 年龄≤35岁中,PPOS组、LP组、AP组的年龄、不孕年限、BMI、bE₂、bP、bLH之间,差异无统计学意义,PPOS组bFSH高于LP组和AP组,bFSH/bLH高于AP组,差异有统计学意义(P<0.05)。年龄>35岁组中,PPOS组与LP组、AP组在年龄、不孕年限、BMI、bE₂、bP、bLH、bFSH/bLH之间,差异无统计学意义,PPOS组和AP组的bFSH水平高于LP组,差异有统计学意义(P<0.05)。见表1。

2.2 3组促排卵数据比较 年龄≤35岁组中,PPOS组和LP组的Gn总剂量高于AP组,PPOS组和AP组的Gn天数少于LP组,但两组HCG日的LH水平高于LP组(P<0.05)。此外,PPOS组HCG日的E₂和P水平低于其他两组(P<0.05)。年龄>35岁组中,PPOS组和AP组在Gn总剂量和Gn总天数方面均低于LP组,后者HCG日LH较前两组减小(P<0.05)。此外,PPOS组HCG日E₂小于LP组(P<0.05),与AP组差异不大。同时PPOS组HCG日P均低于LP组和AP组(P<0.05)。见表2。

2.3 3组实验室参数比较 年龄≤35岁组中,PPOS组的获卵总数、MII卵数、2PN受精数、卵裂数、2PN卵裂数、囊胚形成数、优质胚胎数、高评分囊胚数、可移植胚胎数、冷冻胚胎数、囊胚检测数、整倍体

表1 三组患者的一般资料比较 [M(P₂₅, P₇₅)]

Tab. 1 Comparison of basal characteristics among the three groups [M(P₂₅, P₇₅)]

Item	≤35 years					>35 years				
	PPOS group (n=48)	LP group (n=160)	AP group (n=220)	χ ² value	P value	PPOS group (n=60)	LP group (n=57)	AP group (n=111)	χ ² value	P value
Age (years)	32.5 (30.0,34.0)	31.0 (29.0,33.0)	31 (29.0,33.0)	5.65	0.059	40.0 (38.0,41.0)	39.0 (37.0,40.0)	39.0 (37.0,40.0)	4.06	0.131
Infertility duration (years)	3.0(1.0,5.0)	2.0(1.0,3.0)	2.0(1.0,4.0)	1.59	0.452	2.0(1.0,4.0)	3.0(1.0,4.0)	2.0(1.0,4.0)	0.44	0.803
BMI (kg/m ²)	21.2 (20.3,22.5)	22.0 (20.2,23.6)	22.1 (19.9,24.0)	3.11	0.211	22.3 (21.5,24.1)	22.7 (21.5,25.2)	22.4 (20.8,24.4)	1.80	0.406
bFSH (IU/L)	7.9 (6.3,9.2) ^{b,c}	6.6 (5.7,7.8) ^a	6.5 (5.6,7.8) ^a	9.95	0.007	7.8 (6.7,10.0) ^b	7.1 (5.9,7.9) ^{a,c}	7.9 (6.3,9.4) ^b	9.07	0.011
bE ₂ (pmol/L)	169.0 (103.7,268.1)	139.9 (92.3,199.8)	125.3 (91.7,190.6)	5.39	0.068	206.0 (130.0,251.0)	164.1 (104.5,246.0)	168.8 (94.4,265.0)	3.07	0.216
bP (nmol/L)	1.4(0.6,2.2)	1.4(0.8,2.3)	1.3(0.7,2.4)	0.69	0.707	1.3(0.8,2.7)	1.4(0.5,2.7)	1.3(0.6,2.5)	0.00	0.999
bLH (IU/L)	4.5(2.9,6.0)	4.6(3.2,5.9)	4.7(3.4,6.6)	1.10	0.577	4.3(2.5,5.6)	3.7(2.7,5.6)	4.4(3.4,5.8)	5.82	0.055
bFSH/bLH	1.8(1.3,2.5) ^c	1.5(1.1,2.1)	1.4(1.1,2.1) ^a	7.63	0.022	2.1(1.5,3.2)	1.9(1.3,2.5)	1.8(1.4,2.4)	5.34	0.069

^aP<0.05 vs PPOS group; ^bP<0.05 vs LP group; ^cP<0.05 vs AP group.

表 2 3组周期参数的比较 [M(P₂₅,P₇₅)]

Tab. 2 Comparison of cycle parameters among the three groups [M(P₂₅,P₇₅)]

Item	≤35 years					>35 years				
	PPOS group (n=48)	LP group (n=160)	AP group (n=220)	χ ² value	P value	PPOS group (n=60)	LP group (n=57)	AP group (n=111)	χ ² value	P value
Total Gn dosage(IU)	2 175.0 (1 600.0, 2 500.0) ^c	2 475.0 (1 975.0, 3 000.0) ^c	1 800.0 (1 575.0, 2 250.0) ^{a,b}	60.768	<0.001	2 525.0 (1 987.5, 3 000.0) ^b	3000.0 (2 456.3, 3 750.0) ^{a,c}	2 400.0 (2 000.0, 3 018.8) ^b	20.303	<0.001
Total Gn duration (days)	8.0 (7.0,9.0) ^b	11.0 (10.0,12.0) ^{a,c}	9.0 (8.0,10.0) ^b	178.206	<0.001	9.0 (7.0,10.0) ^b	11.0 (11.0,12.0) ^{a,c}	9.0 (8.0,10.0) ^b	87.039	<0.001
E ₂ on hCG day (pmol/L)	5 725.5 (3 750.5, 9 173.3) ^{b,c}	9 579.7 (5 322.8, 16 856.8) ^a	8 471.2 (5 349.6, 15 216.2) ^a	14.191	0.001	6 239.5 (3 792.0, 8 260.3) ^b	8 400.0 (5 097.5, 16 367.4) ^a	6 372.0 (3 997.0, 9 438.1)	8.485	0.014
LH on hCG day (IU/L)	2.6 (1.5,4.5) ^b	1.6 (1.1,2.4) ^{a,c}	2.6 (1.5,3.8) ^b	40.948	<0.001	3.0 (2.1,4.6) ^b	1.2 (1.0,2.0) ^{a,c}	2.8 (1.8,4.4) ^b	52.340	<0.001
P on hCG day (nmol/L)	2.9 (2.0,6.1) ^{b,c}	3.2 (2.0,4.5) ^a	4.9 (3.2,6.5) ^a	19.577	<0.001	1.8 (1.1,3.0) ^{b,c}	3.0 (2.0,4.2) ^a	2.8 (1.7,3.9) ^a	11.984	0.002

^aP<0.05 vs PPOS group; ^bP<0.05 vs LP group; ^cP<0.05 vs AP group.

数、至少1个整倍体率均小于其余两组(P<0.05),但PPOS组的MII卵率、2PN受精率、卵裂率、2PN卵裂率、囊胚形成率、优质胚胎率、整倍体率与其他两组差异无统计学意义。年龄>35岁组中,PPOS组的MII卵率、2PN卵裂率、囊胚形成率、整倍体数、整倍体率、至少1个整倍体率差异无统计学意义。然而,PPOS组和AP组的获卵总数、MII卵数、2PN受精数、卵裂数、2PN卵裂数均低于LP组(P<0.05)。PPOS组的卵裂率高于LP组和AP组(P<0.05),但优胚数、高评分囊胚数、囊胚检测数均低于LP组和AP组(P<0.05)。PPOS组的2PN受精率明显高于AP组(P<0.05),优胚率明显低于AP组(P<0.05)。且PPOS组囊胚形成数、可移植胚胎数、冷冻胚胎数明显低于LP组(P<0.05),见表3。

2.4 3组首次冻融胚胎移植(frozen embryo transfer, FET)结局比较 共计419个周期进行了首次胚胎移植。统计学分析显示,PPOS组行首次FET时的年龄高于其余2组(P<0.05),但3组的生化妊娠率、临床妊娠率、活产率、早期流产率及晚期流产率差异均无统计学意义,见表4。由于3组间基线年龄存在显著差异,而年龄是影响妊娠结局的已知独立因素,因此在进行多元Logistic回归分析时,课题组将年龄作为协变量纳入模型以控制其混杂效应。在平衡年龄因素后,生化妊娠率和临床妊娠率与促排卵方案仍无相关性,见表5。

3 讨论

控制性卵巢刺激(controlled ovarian stimulation, COS)通过外源性Gn诱导多个窦卵泡同步发育,已成为提升IVF周期活产率的核心策略^[9]。然而,多卵泡同步生长引发的血清E₂水平显著升高会刺激垂体提前分泌LH,形成早发性LH峰,最终可能导致卵泡自发排卵^[10],这一现象是COS实施中的关键挑战。GnRH类似物可通过拮抗内源性LH分泌,有效预防早发性LH峰的发生,并降低周期取消率^[11]。作为辅助生殖技术的核心环节,目前临床中最常用的COS方案包括黄体期长方案与拮抗剂方案。黄体期长方案通过GnRH激动剂提前抑制垂体,促进卵泡同步发育^[12]。但Gn用量大、OHSS风险高且治疗周期长。拮抗剂方案缩短治疗周期时长、降低OHSS风险^[13],但存在卵泡发育同步性较差、获卵数相对较少,子宫内膜容受性低等问题^[14]。

在此研究背景下,学者们开始聚焦高孕激素状态对下丘脑-垂体-卵巢轴的特异性调控机制。Kuang et al^[3]于2015年正式提出PPOS方案,其核心机制是通过外源性孕激素作用于下丘脑孕激素受体,下调LHCGR-PGR通路,降低GnRH脉冲频率,从而有效抑制内源性LH峰^[9]。该方案联合促性腺激素可同步募集多个卵泡,具有用药量少、性价比高、OHSS风险低等优势^[4, 15],尤其适用于卵巢储备功能减退(diminished ovarian reserve, DOR)、高龄及

表3 3组促排结局的比较 [M(P₂₅,P₇₅), n(%)]

Tab. 3 Comparison of controlled ovarian stimulation outcomes among the three groups [M(P₂₅,P₇₅), n(%)]

Item	≤35 years					>35 years				
	PPOS group (n=48)	LP group (n=160)	AP group (n=220)	χ ² value	P value	PPOS group (n=60)	LP group (n=57)	AP group (n=111)	χ ² value	P value
Total oocytes retrieved	7.0 (5.0,12.0) ^{b,c}	15.0 (10.0,20.0) ^a	12.0 (8.0,19.0) ^a	36.688	<0.001	6.0 (4.0,9.0) ^b	11.0 (7.0,16.5) ^{a,c}	7.0 (4.0,10.0) ^b	25.011	<0.001
Number of MII oocytes	5.0 (4.0,9.0) ^{b,c}	11.5 (8.0,15.8) ^{a,c}	9.0 (6.0,15.0) ^{a,b}	41.945	<0.001	5.0 (3.0,8.0) ^b	8.0 (5.0,13.0) ^{a,c}	6.0 (3.0,9.0) ^b	19.266	<0.001
MIIOocyte rate (%)	76.1 (318/418)	79.4 (1980/2494) ^c	75.8 (2400/3167) ^b	10.723	0.005	83.9 (328/391)	80.5 (558/693)	81.9 (788/962)	1.917	0.383
Number of 2 PN zygotes	4.0 (3.0,6.0) ^{b,c}	8.0 (6.0,12.0) ^a	7.0 (5.0,11.0) ^a	34.027	<0.001	4.0 (2.0,6.0) ^b	6.0 (3.5,9.0) ^{a,c}	4.0 (2.0,7.0) ^b	10.708	0.005
2 PN fertilization rate	72.3 (230/318)	74.5 (1476/1980)	75.7 (1816/2400)	1.995	0.369	77.7 (255/328) ^c	71.1 (397/558)	70.6 (556/788) ^a	6.382	0.041
Cleavage number	5.0 (3.0,8.0) ^{b,c}	10.0 (7.0,14.0) ^{a,c}	8.0 (5.0,13.0) ^{a,b}	41.920	<0.001	4.0 (3.0,7.0) ^b	7.0 (4.0,11.0) ^{a,c}	5.0 (3.0,8.0) ^b	13.912	0.001
Cleavage rate	84.3 (268/318)	88.0 (1743/1980)	86.8 (2083/2400)	3.988	0.136	93.3 (306/328) ^{b,c}	85.1 (475/558) ^a	86.4 (681/788) ^a	13.584	0.001
Number of cleaved 2 PN embryos	4.0 (2.0,6.0) ^{b,c}	8.0 (5.8,12.0) ^a	4.0 (3.0,7.0) ^a	33.961	<0.001	3.5 (2.0,6.0) ^b	6.0 (3.0,9.0) ^{a,c}	4.0 (2.0,7.0) ^b	10.797	0.005
2 PN cleavage rate	97.8 (225/230)	97.6 (1441/1476)	97.7 (1774/1816)	0.038	0.981	98.8 (252/255)	99.0 (393/397)	98.9 (550/556)	0.179	1.000 (Fisher)
Number of blastocysts formed	2.0 (1.0,5.0) ^{b,c}	6.0 (4.0,9.0) ^a	4.0 (3.0,8.0) ^a	32.407	<0.001	2.0 (1.3,3.8) ^b	3.0 (2.0,5.0) ^a	3.0 (2.0,4.0)	9.023	0.011
Blastocysts formed rate	58.2 (156/268)	58.3 (1017/1743)	59.5 (1240/2083)	0.611	0.737	52.6 (161/306)	48.8 (232/475) ^c	56.5 (385/681) ^b	6.707	0.035
Number of high-quality embryos	2.0 (1.0,4.0) ^{b,c}	5.0 (3.0,8.0) ^a	4.0 (2.0,7.0) ^a	30.946	<0.001	1.5 (1.0,3.0) ^{b,c}	3.0 (1.0,4.0) ^a	2.0 (1.0,4.0) ^a	13.307	0.001
High-quality embryo rate	50.4 (116/230)	56.9 (840/1476)	55.5 (1008/1816)	3.483	0.175	43.5 (111/255) ^c	48.4 (192/397)	55.0 (306/556) ^a	10.254	0.006
Number of high-grade blastocysts	2.0 (1.0,4.0) ^{b,c}	5.0 (3.0,8.0) ^a	4.0 (2.0,7.0) ^a	28.271	<0.001	2.0 (1.0,3.0) ^{b,c}	3.0 (1.0,4.0) ^a	2.0 (1.0,4.0) ^a	12.039	0.002
Number of transferable embryos	2.0 (1.0,5.0) ^{b,c}	6.0 (4.0,9.0) ^a	4.0 (3.0,8.0) ^a	33.822	<0.001	2.0 (1.0,3.8) ^b	3.0 (2.0,5.0) ^a	3.0 (2.0,4.0)	8.842	0.012
Number of cryopreserved embryos	2.0 (1.0,5.0) ^{b,c}	6.0 (4.0,9.0) ^{a,c}	4.0 (3.0,8.0) ^{a,b}	34.328	<0.001	2.0 (1.0,3.8) ^b	3.0 (2.0,5.0) ^a	3.0 (2.0,4.0)	8.312	0.016
Number of blastocysts biopsied	2.0 (1.0,4.0) ^{b,c}	6.0 (4.0,9.0) ^a	5.0 (3.0,8.0) ^a	37.583	<0.001	2.0 (1.0,3.0) ^{b,c}	3.0 (2.0,5.0) ^a	3.0 (2.0,4.0) ^a	11.794	0.003
Number of euploid embryos	1.0 (0.0,1.0) ^{b,c}	1.0 (1.0,3.0) ^a	1.0 (1.0,3.0) ^a	20.026	<0.001	0.0 (0.0,1.0)	0.0 (0.0,2.0)	0.0 (0.0,1.0)	3.747	0.154
Euploidy rate (%)	26.2 (38/145)	31.6 (313/989)	31.4 (375/1194)	1.801	0.406	19.3 (28/145)	25.1 (57/227)	20.7 (79/381)	2.241	0.326
Rate of ≥1 euploid embryo per case	52.1 (25/48) ^{b,c}	80.0 (128/160) ^a	71.4 (157/220) ^a	14.668	0.001	38.3 (23/60)	49.1 (28/57)	42.3 (47/111)	1.425	0.491

^aP < 0.05 vs PPOS group; ^bP < 0.05 vs LP group; ^cP < 0.05 vs AP group.

表 4 3组移植结局比较 [$M(P_{25}, P_{75}), n(\%)$]

Tab. 4 Comparison of transfer outcomes among the three groups [$M(P_{25}, P_{75}), n(\%)$]

Item	PPOS group (n=45)	LP group (n=160)	AP group (n=214)	χ^2 value	P value
Age (years)	37.0 (32.5, 40.0) ^{b,c}	32.0 (30.0, 35.0) ^a	33.0 (30.0, 36.0) ^a	16.700	<0.001
Endometrial preparation protocol					
Natural cycle	2	5	6		
Hormone replacement cycle	43	154	208		
Down-regulation + hormone replacement cycle	0	1	0		
Biochemical pregnancy rate	77.8 (35/45)	68.1 (109/160)	69.6 (149/214)	1.575	0.455
Clinical pregnancy rate	68.9 (31/45)	60.6 (97/160)	62.1 (133/214)	1.025	0.599
Live birth rate	90.3 (28/31)	87.6 (85/97)	91.0 (121/133)	0.735 (Fisher)	0.740
Early miscarriage rate	6.5 (2/31)	10.3 (10/97)	6.8 (9/133)	1.015 (Fisher)	0.586
Late miscarriage rate	3.2 (1/31)	2.1 (2/97)	2.2 (3/133)	0.609 (Fisher)	0.724

^a $P < 0.05$ vs PPOS group; ^b $P < 0.05$ vs LP group; ^c $P < 0.05$ vs AP group.

表 5 影响生化妊娠率及临床妊娠率相关因素的多元 Logistic 回归分析

Tab. 5 Multivariate Logistic regression analysis of factors influencing biochemical pregnancy rate and clinical pregnancy rate

Parameters associated with biochemical pregnancy rate	OR (95%CI)	P value	Parameters associated with clinical pregnancy rate	OR (95%CI)	P value
Age (years)	0.973 (0.890–0.986)	0.012	Age (years)	0.964 (0.919–1.011)	0.130
COS protocols			COS protocols		
LP protocol vs PPOS protocol	0.495 (0.222–1.107)	0.087	LP protocol vs PPOS protocol	0.613 (0.295–1.275)	0.190
AP protocol vs PPOS protocol	0.539 (0.246–1.179)	0.122	AP protocol vs PPOS protocol	0.645 (0.316–1.315)	0.228

反复种植失败患者。但是,大量孕激素会导致子宫内膜提前进入分泌期,与胚胎发育不同步,无法行鲜胚移植。

本研究在同一队列中系统比较了PPOS方案、黄体期长方案和拮抗剂方案3种促排卵方案的实验室指标与临床结局,并按年龄分层分析(≤ 35 岁组 vs > 35 岁组),更清晰地揭示了各方案在不同人群中的优势与局限。此外,本研究不仅关注实验室参数,还追踪了不同方案下胚胎的首次冻融移植结局(包括生化妊娠率、临床妊娠率、活产率及流产率),为评估PPOS方案的临床有效性提供了更完整的循证依据。

在实验室指标方面,本研究的年龄分层分析具有重要临床启示。对于年轻女性(≤ 35 岁),尽管PPOS方案在获卵总数、成熟卵母细胞数、受精数及囊胚数上低于传统方案,但其在受精率、卵裂率、优质胚胎率及整倍体率上与传统方案无显著差异,表明该方案对卵子质量及胚胎发育潜能未造成明显损害。然而,由于获卵数较少,PPOS组每个周期获得至少1个整倍体胚胎的概率显著降低。这一发现对拟行胚胎植入前PGT-A的年轻患者尤为重要——即便单个胚胎质量不受影响,累积足够数量的

整倍体胚胎可能需要多个促排卵周期,增加了时间与成本。这提示在年轻且需行PGT-A的人群中,选择获卵数更有保障的方案可能更具优势。

对于高龄女性(> 35 岁),PPOS方案在获卵总数、成熟卵母细胞数及囊胚形成数上亦显著低于黄体期长方案,但与拮抗剂方案相比则无显著差异,这反映出在高龄且卵巢储备下降的人群中,低强度刺激方案的局限性。值得注意的是,PPOS组的卵裂率显著高于另外2组,2PN受精率也优于AP组,提示孕激素环境可能对部分胚胎早期发育指标有正向影响,但其优质胚胎率低于拮抗剂方案。在高龄女性最为关注的染色体整倍体方面,3组间胚胎整倍体率及至少1个整倍体率均无显著差异,进一步证实了PPOS方案在染色体安全性上的可靠性。更关键的是,尽管PPOS组患者年龄偏大,其首次冻融移植周期的生化妊娠率、临床妊娠率、活产率及流产率与其他两组无显著差异,表明该方案能为高龄女性提供有效的妊娠机会。

综上所述,PPOS方案为卵巢正常反应及高反应人群、需灵活安排周期的患者提供了一种OHSS风险低、治疗时间短的替代方案,尤其对高龄女性而言,它能在保障妊娠结局的同时简化治疗流程。然

而对于获卵总数依赖性强、需要累积足够整倍体胚胎的 PGT-A 患者,特别是年轻女性,传统方案在获卵效率上仍具优势。因此,临床实践中应结合卵巢储备、年龄及治疗目标(如是否行 PGT-A)进行个体化选择,以平衡周期累积效率、安全性与经济成本。

参考文献

- [1] Carvalho F, Coonen E, Goossens V, et al. ESHRE PGT Consortium good practice recommendations for the organisation of PGT [J]. *Hum Reprod Open*, 2020, 2020 (3): hoaa021. doi: 10.1093/hropen/hoaa021.
- [2] Demko Z P, Simon A L, McCoy R C, et al. Effects of maternal age on euploidy rates in a large cohort of embryos analyzed with 24-chromosome single-nucleotide polymorphism-based preimplantation genetic screening [J]. *Fertil Steril*, 2016, 105(5): 1307-13. doi:10.1016/j.fertnstert.2016.01.025.
- [3] Kuang Y, Chen Q, Fu Y, et al. Medroxyprogesterone acetate is an effective oral alternative for preventing premature luteinizing hormone surges in women undergoing controlled ovarian hyperstimulation for *in vitro* fertilization [J]. *Fertil Steril*, 2015, 104(1): 62-70. e3. doi:10.1016/j.fertnstert.2015.03.022.
- [4] Zhang J, Du M, Zhang C, et al. Cumulative live birth rate in mild versus conventional stimulation in progestin-primed ovarian stimulation protocols for individuals with low prognosis [J]. *Front Endocrinol*, 2023, 14: 1249625. doi: 10.3389/fendo.2023.1249625.
- [5] Pai A H, Sung Y J, Li C J, et al. Progestin Primed Ovarian Stimulation (PPOS) protocol yields lower euploidy rate in older patients undergoing IVF [J]. *Reprod Biol Endocrinol*, 2023, 21(1): 72. doi:10.1186/s12958-023-01124-3.
- [6] Wang L, Wang J Y, Zhang Y, et al. Comparison of the euploidy rate in preimplantation genetic testing for aneuploidy cycles following progestin-primed versus gonadotropin-releasing hormone antagonist protocol: a randomized controlled study [J]. *Reprod Biol Endocrinol*, 2025, 23(1): 67. doi:10.1186/s12958-025-01404-0.
- [7] 周海燕, 吴彩云, 黄德煊, 等. 生长激素预处理在胚胎植入前染色体非整倍体检测中的应用研究 [J]. *安徽医科大学学报*, 2024, 59(6): 988-93. doi: 10.19405/j.cnki.issn1000-1492.2024.06.012.
- [7] Zhou H Y, Wu C Y, Huang D H, et al. Application of growth hormone pretreatment in preimplantation genetic testing for aneuploidy [J]. *Acta Univ Med Anhui*, 2024, 59(6): 988-93. doi: 10.19405/j.cnki.issn1000-1492.2024.06.012.
- [8] 李珊, 黄钰, 胡凯伦, 等. 胚胎植入前非整倍体遗传学检测患者血清抗苗勒管激素水平与囊胚整倍体率的相关性研究 [J]. *中华生殖与避孕杂志*, 2023, 43(5): 483-9. doi:10.3760/cma.j.cn101441-20221103-00482.
- [8] Li S, Huang S, Hu K L, et al. Relationship between serum anti-Müllerian hormone and rate of euploid blastocysts in patients undergoing preimplantation genetic testing for aneuploidies (PGT-A) [J]. *Chin J Reprod Contracep*, 2023, 43(5): 483-9. doi: 10.3760/cma.j.cn101441-20221103-00482.
- [9] Del Mar Vidal M, Martínez F, Rodríguez I, et al. Ovarian response and embryo ploidy following oral micronized progesterone-primed ovarian stimulation versus GnRH antagonist protocol. A prospective study with repeated ovarian stimulation cycles [J]. *Hum Reprod*, 2024, 39(5): 1098-104. doi: 10.1093/humrep/deac047.
- [10] 鲍妍婧, 李海燕, 刘敏茵, 等. 高孕激素状态下促排卵在多囊卵巢综合征中应用的机制及研究进展 [J]. *中华生殖与避孕杂志*, 2024, 44(9): 963-7. doi: 10.3760/cma.j.cn101441-20231024-00174.
- [10] Bao Y J, Li H Y, Liu M Y, et al. Mechanism and progress for progestin-primed ovarian stimulation protocol in the patients with polycystic ovary syndrome [J]. *Chin J Reprod Contracep*, 2024, 44(9): 963-7. doi: 10.3760/cma.j.cn101441-20231024-00174.
- [11] Bosch E, Broer S, Griesinger G, et al. ESHRE guideline: ovarian stimulation for IVF/ICSI [J]. *Hum Reprod Open*, 2020, 2020(2): hoaa009. doi:10.1093/hropen/hoaa009.
- [12] 范咏琪, 张文香, 章志国. 不同年龄段人群三种促排卵方案胚胎发育及临床结局比较 [J]. *四川大学学报(医学版)*, 2024, 55(3): 580-7. doi: 10.12182/20240560508.
- [12] Fan Y Q, Zhang W X, Zhang Z G. Comparative study of the embryo development and clinical outcomes of 3 ovarian stimulation protocols in different age groups [J]. *J Sichuan Univ Med Sci*, 2024, 55(3): 580-7. doi: 10.12182/20240560508.
- [13] 中国女医师协会生殖医学专业委员会专家共识编写组, 李蓉, 甄秀梅, 等. 辅助生殖领域拮抗剂方案标准化应用专家共识 [J]. *中华生殖与避孕杂志*, 2022, 42(2): 109-16. doi: 10.3760/cma.j.cn101441-20211108-00495.
- [13] Expert Consensus Compilation Group of Reproductive Medicine Committee of China Medical Women's Association, Li R, Zhen X M, et al. Expert consensus on standardized application of antagonist protocol in assisted reproductive technology [J]. *Chin J Reprod Contracep*, 2022, 42(2): 109-16. doi:10.3760/cma.j.cn101441-20211108-00495.
- [14] He Z, Guo N, Yao Y, et al. The effects of GnRH analogues on endometrial receptivity: a comprehensive study [J]. *J Assist Reprod Genet*, 2025, 42(7): 2313-23. doi: 10.1007/s10815-025-03495-5.
- [15] 李彩华, 郭培培, 姜小花, 等. 卵泡期高孕激素状态下促排卵方案的应用进展 [J]. *国际生殖健康/计划生育杂志*, 2024, 43(1): 68-73. doi:10.12280/gjszjk.20230476.
- [15] Li C H, Guo P P, Jiang X H, et al. Application progress of progestin-primed ovarian stimulation [J]. *J Int Reprod Health/family Plan*, 2024, 43(1): 68-73. doi:10.12280/gjszjk.20230476.

Analysis of the impact of high progesterone ovulation induction protocols on embryo euploidy rates and clinical pregnancy outcomes in infertile patients

Wang Minjie¹, Zhang Yongjing¹, Qian Jin¹, Wang Chao^{1,2,3}, Xu Yuping^{1,2,3},

Wang Tianjuan^{1,2,3}, Chen Dawei^{1,4,5}, Hao Yan^{1,4,5}, Xing Qiong^{1,2,3}

(¹Department of Obstetrics and Gynecology, The First Affiliated Hospital of Anhui Medical University, Hefei 230022; ²NHC Key Laboratory of Research on Gametogenesis and Reproductive Tract Abnormalities, Hefei 230022; ³Key Laboratory of Population Health Across Life Cycle, Ministry of Education, Anhui Medical University, Hefei 230032; ⁴Engineering Research Center of Life Resources Preservation and Artificial Organs, Ministry of Education, Anhui Province, Hefei 230032; ⁵Anhui Provincial Key Laboratory of Reproductive Health and Genetics, Hefei 230032)

Abstract Objective To analyze the effects of the progestin-primed ovarian stimulation (PPOS) protocol on embryo euploidy rate and clinical pregnancy outcomes in infertile patients. **Methods** Women who underwent Preimplantation genetic testing for aneuploidy (PGT-A) cycles were selected as study participants (a total of 656 cycles and 3 081 blastocysts). Participants were divided into two age groups (≤ 35 years and > 35 years) and further stratified by ovarian stimulation protocol: the Progestin-Primed Ovarian Stimulation (PPOS) group ($n=48$ and 60 , respectively), the Luteal Phase Long Protocol (LP) group ($n=160$ and 57 , respectively), and the Gonadotropin-Releasing Hormone Antagonist Protocol (AP) group ($n=220$ and 111 , respectively). Baseline characteristics, ovarian stimulation outcomes, and embryo development parameters were compared among the three protocols within each age group. Additionally, clinical pregnancy outcomes of the first frozen embryo transfer (FET) cycle were compared. The primary outcome measure was the embryo euploidy rate. **Results** ① In the ≤ 35 years age group, baseline follicle-stimulating hormone (bFSH) levels were significantly higher in the PPOS group compared to the LP and AP groups, and the bFSH/bLH ratio was significantly higher in the PPOS group than in the AP group ($P < 0.05$). In the > 35 years age group, bFSH levels in both the PPOS and AP groups were significantly higher than in the LP group ($P < 0.05$). ② In the ≤ 35 years group, there were no significant differences in the rates of metaphase II (MII) oocytes, 2-pronuclei (2 PN) zygotes, cleavage, 2 PN cleavage, blastocyst formation, high-quality embryos, or embryo euploidy between the PPOS group and either the LP or AP groups. However, the PPOS group showed significantly lower values for the following parameters compared to the other two groups: total oocytes retrieved, number of MII oocytes, number of 2 PN zygotes, number of cleaved embryos, number of 2 PN cleaved embryos, number of blastocysts formed, number of high-quality embryos, number of high-grade blastocysts, number of transferable embryos, number of cryopreserved embryos, number of biopsied blastocysts, number of euploid embryos, and the rate of obtaining at least one euploid embryo. In the > 35 years group, no significant differences were observed among the PPOS, LP, and AP groups in the rates of MII oocytes, 2 PN cleavage, blastocyst formation, or in the number of euploid embryos, euploidy rate, and the rate of obtaining at least one euploid embryo. However, the PPOS group had significantly lower numbers of total oocytes retrieved, MII oocytes, 2 PN zygotes, cleaved embryos, 2 PN cleaved embryos, blastocysts formed, transferable embryos, and cryopreserved embryos compared to the LP group ($P < 0.05$). The high-quality embryo rate was significantly lower in the PPOS group than in the AP group ($P < 0.05$). The numbers of high-quality embryos, high-grade blastocysts, and biopsied blastocysts were significantly lower in the PPOS group than in both the LP and AP groups ($P < 0.05$). Notably, the 2 PN fertilization rate was significantly higher in the PPOS group than in the AP group, and the cleavage rate was significantly higher in the PPOS group than in both the LP and AP groups ($P < 0.05$). ③ No significant differences

网络出版时间:2026-04-11 14:33:34 网络出版地址:https://link.cnki.net/urlid/34.1065.R.20260411.1245.004

EDNRA 基因多态性与汉族男性先天性双侧输精管缺如的相关性研究

彭玉婉¹, 贺小进², 杨晓玉³, 王晶⁴, 王彬彬⁴, 汤冬冬⁵, 魏兆莲⁵, 曹云霞⁵

(安徽医科大学第一附属医院¹妇产科、⁵生殖医学中心,合肥 230022;²上海市第一人民医院生殖医学中心,上海 200080;³江苏省人民医院生殖医学中心,南京 210009;
⁴国家人口计划生育研究所,北京 100081)

摘要 目的 探究内皮素 A 型受体基因(*EDNRA*)与先天性双侧输精管缺如(CBAVD)之间的关联。方法 收集汉族男性 124 例患有 CBAVD 病例人群和 100 例健康汉族对照人群。采用聚合酶链反应-限制性片段长度多态性技术(PCR-RFLP)和直接测序方法检测 *EDNRA* 基因中的两个单核苷酸多态性位点(rs5335,rs1801708)在两组人群中的频率分布。结果 两个多态性位点的等位基因、基因型频率在两组间差异无统计学意义(rs1801708: $P=0.2202, 0.1632$;rs5335: $P=0.8058, 0.8186$),单倍型 rs1801708-rs5335 AG 在两组中差异有统计学意义($P=0.0086, OR=2.178, 95\% CI: 1.207\sim 3.929$),单倍型 rs1801708-rs5335 GG 在两组中差异也有统计学意义($P=0.0385, OR=0.671, 95\% CI: 0.460\sim 0.980$),Bonferroni 校正后结果单倍型 A-G $P=0.0086 < 0.0125$,仍然显著,单倍型 G-G 不显著。结论 *EDNRA* 单倍型 rs1801708-rs5335 AG 与 CBAVD 的发生发展有正相关性。

关键词 输精管/畸形;先天性双侧输精管缺如;内皮素受体 A 基因;单核苷酸多态性;单倍型;汉族男性

中图分类号 R 697.25

文献标志码 A **文章编号** 1000-1492(2026)05-0931-06

doi:10.19405/j.cnki.issn1000-1492.2026.05.018

先天性双侧输精管缺如(congenital bilateral absence of the vas deferens, CBAVD)是导致梗阻性无精子症(obstructive azoospermia, OA)的主要原因之一,作为囊性纤维化(cystic fibrosis, CF)的孤立性生殖系统表型^[1],其发生发展与囊性纤维化跨膜传导调节因子(cystic fibrosis transmembrane conductance

regulator, *CFTR*)基因的突变存在密切关联^[2],且存在显著种族差异:高加索人群 *CFTR* 突变检出率高,而以汉族为代表的亚洲人群突变检出率低、突变类型独特^[2-3],仍有部分 CBAVD 患者未检测到明确的 *CFTR* 突变^[4],提示非 *CFTR* 基因及环境因素参与疾病发生^[5]。目前已有研究证实 *ADGRG2*^[4]等非 *CFTR* 基因与 CBAVD 相关,内皮素 A 型受体基因(endothelin receptor type A gene, *EDNRA*)作为 CF 相关易感基因,其多态性与欧洲、印度人群 CBAVD 发病相关^[5-6],且可调控细胞增殖、炎症反应等生理过程^[7],

2026-02-26 接收

基金项目:安徽省高校科研计划项目(编号:2024AH030028)

作者简介:彭玉婉,女,硕士研究生,主治医师;

曹云霞,女,教授,主任医师,博士生导师,通信作者, E-mail:caoyunxia6@126.com

were found among the three groups in the biochemical pregnancy rate, clinical pregnancy rate, live birth rate, early miscarriage rate, and late miscarriage rate following the first FET cycle. **Conclusion** Compared to the other two protocols, the PPOS protocol does not significantly affect embryo euploidy or clinical pregnancy rates. However, in freeze-all cycles with PGT-A, the PPOS protocol does not reduce the rate of chromosomally normal embryos but may decrease the total number of available embryos. It may not be the optimal choice for younger women, but it can be considered as a viable option for women of advanced maternal age.

Key words progestin-primed ovarian stimulation protocol; luteal phase long protocol; antagonist Protocol; embryo euploidy rate; frozen-thawing embryo transfer

Fund program Research Project of Anhui Provincial Institute of Translational Medicine (No. 2023zhyx-C38)

Corresponding author Xing Qiong, E-mail: joan2004207@163.com