

doi: 10.13241/j.cnki.pmb.2022.08.013

胚胎移植术前指导患者憋尿对移植结局影响的研究*

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摘要 目的:探讨胚胎移植术前患者憋尿准备的细化指导方法,并分析其对患者移植结局的影响。**方法:**选取 2019 年 9 月至 2020 年 12 月期间我院收治的 194 例胚胎移植患者(包括新鲜周期胚胎移植和冻融周期胚胎移植),按随机数字表法分为指导组(101 例)和对照组(93 例)。对照组患者给予常规指导憋尿,指导组患者在对照组的基础上给予更细化的憋尿指导方法。比较两组总妊娠率、不同年龄段患者的移植妊娠率,分析提前指导憋尿对瘢痕子宫和无子宫手术史患者移植妊娠率的影响。**结果:**指导组总妊娠率为 59.41%,对照组总妊娠率为 53.76%,指导组总妊娠率高于对照组,但是未见显著性差异($P>0.05$);在<35 岁的患者中,指导组妊娠率(76.47%)高于对照组(58.33%),差异有统计学意义($P<0.05$);在瘢痕子宫和无子宫手术史的患者中,两组移植妊娠率比较未见显著性差异($P>0.05$)。**结论:**胚胎移植术前给予患者细化的憋尿指导方法能提高<35 岁患者的移植妊娠率,对瘢痕子宫和无子宫手术史患者的移植妊娠率无明显影响。

关键词: 胚胎移植;憋尿;移植结局

中图分类号: R321.33 **文献标识码:** A **文章编号:** 1673-6273(2022)08-1466-04

Study on the Effect of Guiding Patients to Hold Back Urine before Embryo Transfer on the Outcome of Embryo Transfer*

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ABSTRACT Objective: To explore the detailed guidance method of hold back urine preparation before embryo transfer, and to analyze the impact on the outcome of embryo transfer. **Methods:** 194 patients with embryo transfer (including fresh cycle embryo transfer and freeze-thaw cycle embryo transfer) who were treated in our hospital from September 2019 to December 2020 were selected, they were divided into guidance group (101 cases) and control group (93 cases) according to the random number table method. The patients in the control group were given routine guidance to hold back urine, and the patients in the guidance group was given more detailed guidance methods to hold back urine on the basis of the control group. The total pregnancy rate, transplant pregnancy rate of patients of different ages were compared between the two groups. The effect of early guidance to hold urine on the pregnancy rate of transplantation in patients with scar uterus and patients without uterine surgery history was analyzed. **Results:** The total pregnancy rate was 59.41% in the guidance group, and 53.76% in the control group. The total pregnancy rate in the guidance group was higher than that in the control group, but there was no significant difference ($P>0.05$). In patients < 35 years old, the pregnancy rate in the guidance group (76.47%) was higher than that in the control group (58.33%), the difference was statistically significant ($P<0.05$). In patients with scar uterus and without uterine surgery history, there was no significant difference in the transplantation pregnancy rate between the two groups ($P>0.05$). **Conclusion:** Detailed urine holding guidance before embryo transfer can improve the transplantation pregnancy rate of patients <35 years old, but has no significant effect on the transplantation pregnancy rate of patients with scar uterus and without uterine surgery history.

Key words: Embryo transfer; Hold back urine; Transplant outcome

Chinese Library Classification(CLC): R321.33 **Document code:** A

Article ID: 1673-6273(2022)08-1466-04

前言

1978 年英国剑桥的 Steptoe 和 Edwards 教授通力合作,应用体外受精-胚胎移植技术孕育了世界第一例“试管婴儿”。

这一研究成果为辅助生殖技术的应用开辟了一条崭新的道路,是生殖医学领域的重要里程碑^[1,2]。三十余年来,随着生殖医学及其相关学科研究的不断深入,我国辅助生殖技术逐渐成熟,从经典的体外受精-胚胎移植技术到单精子胞浆内注射(IC-

* 基金项目:上海市自然科学基金项目(17ZR14054120)

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(收稿日期:2021-10-23 接受日期:2021-11-18)

SI)、辅助孵化、囊胚培养、胚胎冷冻(玻璃化冷冻)、卵母细胞冷冻、未成熟卵体外成熟(IVM)、植入前遗传学诊断和胚胎干细胞等技术均得到了广泛的应用和发展^[3,4]。胚胎移植一直以来都是整个体外受精过程中最重要也是最关键的一环,胚胎移植的操作水平极大影响妊娠率^[5,6]。目前我国大多数生殖中心多采取经腹部超声引导下的胚胎移植术^[7]。在移植过程中,超声引导可帮助操作者观察到子宫的位置,确认移植管的置管深度和胚胎是否正确放置^[8]。在胚胎移植术前一般要求患者膀胱的尿量在300~400毫升为佳,不足或过度充盈都会影响经腹超声引导的准确性^[9]。由于个体差异,不同患者肾脏滤过产生尿液的速度以及患者对膀胱憋胀感的敏感程度不尽相同^[10]。常有移植手术时患者主观感觉的膀胱憋胀感与超声显示的膀胱尿量不相符,进而影响移植超声的准确性甚至影响移植效果。本研究通过提前指导患者饮水量及憋尿方法以达到移植当日较理想的膀胱尿量,并探讨提前指导憋尿对移植结局的影响。

1 对象与方法

1.1 研究对象

选取2019年9月至2020年12月期间我院收治的194例胚胎移植患者(包括新鲜周期胚胎移植和冻融周期胚胎移植),按随机数字表法分为指导组(101例)和对照组(93例)。纳入标准:(1)患者基础健康状态良好,符合胚胎移植条件,对本研究知情同意;(2)移植胚胎为优质胚胎(第三天的胚胎有6-10个卵裂球,评分2级以上;或第五天的胚胎评分3BB以上)。排除标准:(1)新鲜周期患者获卵数目>15枚;(2)新鲜周期获卵数目≤15枚,但患者出现卵巢过度刺激症状;(3)合并严重影响子宫大小形态的器质性病变,如弥漫性的子宫腺肌症或直径>5cm的子宫肌瘤;(4)既往膀胱有手术史者。本研究经我院伦理委员会批准。对照组和指导组患者年龄、体质量指数(BMI)、瘢痕子宫、无子宫手术史比例比较均无统计学差异($P>0.05$),具有可比性,见表1。

表1 对照组和指导组患者一般资料

Table 1 General information of patients in control group and guidance group

Groups	n	Age(years)	BMI(kg/m ²)	Scar uterus	Without uterine surgery history
Control group	93	33.40± 5.41	22.33± 2.90	10(10.75%)	83(89.25%)
Guidance group	101	34.40± 5.11	22.46± 3.65	11(10.79%)	90(89.11%)
t/ χ^2		-1.324	-0.273	0.001	0.001
P		0.187	0.785	0.975	0.975

1.2 方法

对照组:患者于移植当天吃早餐,8:00行经阴道超声检查,明确内膜情况后告知患者预计移植时间,嘱患者于移植前2小时排空膀胱后饮用500 mL温水,于10 min内喝完并憋尿。指导组:于移植前一天电话指导患者,嘱患者按照上述方法饮水憋尿2小时后排尿,记录排出的尿液量,如排出尿量在300-400 mL,则视为合格。如排出尿量过多或过少,指导患者于移植当日酌情加减饮水量或调整憋尿时间。

1.3 移植结局统计

患者于胚胎移植后14天通过测定血清 β -HCG数值(>5U/L)判断是否妊娠。

1.4 统计学分析

应用IBM SPSS statistics 22.0软件进行数据统计和分析,计量资料采用均数±标准差描述,组间比较采用t检验;计数资料用例数及百分比描述,组间比较采用 χ^2 检验或Fisher确切概率检验; $P<0.05$ 为差异有统计学意义。

2 结果

2.1 提前指导憋尿对移植结局的影响

指导组妊娠60例,总妊娠率为59.41%,对照组妊娠50例,总妊娠率为53.76%。指导组总妊娠率高于对照组,但是未见显著性差异($P>0.05$),见表2。

表2 提前指导憋尿对移植结局的影响

Table 2 Effect of early guidance hold back urine on the outcome of transplantation

Groups	n	Pregnancy	Without pregnancy	Pregnancy rate(%)
Control group	93	50	43	53.76
Guidance group	101	60	41	59.41
χ^2				0.628
P				0.428

2.2 提前指导憋尿对不同年龄段患者移植结局的影响

基于国内外的相关研究数据,女性从35岁开始生育能力出现明显下降^[11]。在辅助生殖领域,年龄是影响辅助助孕结局

的重要因素之一,年龄大于35岁的患者成功率明显下降^[12]。因此我们引入年龄因素,以35岁为分界进一步分析提前指导憋尿对移植结局的影响,结果如下:首先,本研究共纳入111例

<35 岁的患者,其中指导组 51 例,对照组 60 例。指导组妊娠 39 例,妊娠率为 76.47%,对照组妊娠 35 例,妊娠率为 58.33%,指导组妊娠率高于对照组,差异有统计学意义($P<0.05$)。其次,本研究共纳入 83 例≥ 35 岁的患者,其中指导组 50 例,对照组 33 例。指导组妊娠 21 例,妊娠率为 42.00%,对照组妊娠 15 例,妊娠率为 45.45%,指导组妊娠率低于对照组,该妊娠率差异无统计学意义($P>0.05$),见表 3。

表 3 提前指导憋尿对不同年龄患者移植结局的影响

Table 3 Effect of early guidance of hold back urine on the outcome of transplantation in patients of different ages

Age	Groups	n	Pregnancy	Without pregnancy	Pregnancy rate (%)	χ^2	P
<35 years old	Control group	60	35	25	58.33	4.081	0.043
	Guidance group	51	39	12	76.47		
≥ 35 years old	Control group	33	15	18	45.45	0.097	0.756
	Guidance group	50	21	29	42.00		

2.3 提前指导憋尿对瘢痕子宫患者移植结局的影响

本研究共纳入 21 例瘢痕子宫的患者,其中指导组 11 例,对照组 10 例。指导组妊娠 8 例,妊娠率为 72.73%,对照组妊娠 7 例,妊娠率为 70.00%,两组妊娠率差异无统计学意义($P=0.633$),见表 4。

表 4 提前指导憋尿对瘢痕子宫患者移植结局的影响

Table 4 Effect of early guidance of hold back urine on the outcome of transplantation in patients with scar uterus

Groups	n	Pregnancy	Without pregnancy	Pregnancy rate(%)
Control group	10	7	3	70.00
Guidance group	11	8	3	72.73
P^*				0.633

Note: * Fisher exact probability test was used for inter group comparison.

2.4 提前指导憋尿对无子宫手术史患者移植结局的影响

本研究共纳入 173 例无子宫手术史的患者,其中指导组 90 例,对照组 83 例。指导组妊娠 52 例,妊娠率为 57.78%,对照组妊娠 43 例,妊娠率为 51.81%。对照组妊娠率低于指导组,经统计,该妊娠率差异无统计学意义($P>0.05$),见表 5。

表 5 提前指导憋尿对无子宫手术史患者移植结局的影响

Table 5 Effect of early guidance hold back urine on the outcome of transplantation in patients without uterine surgery history

Groups	n	Pregnancy	Without pregnancy	Pregnancy rate(%)
Control group	83	43	40	51.81
Guidance group	90	52	38	57.78
χ^2				0.622
P				0.430

3 讨论

近年来,随着我国女性平均生育年龄不断推后,同时"二孩政策"、"三孩政策"全面放开,不孕不育发病率持续上升^[13]。辅助生殖的需求不断扩大,辅助生殖的技术也不断进步成熟,体外受精周期数迅速增加,临床妊娠率不断提高^[14-16]。2018 年全国新鲜周期临床妊娠率约为 52.49%[包含体外受精和卵胞浆内单精子注射(ICSI)周期],冻融胚胎复苏移植(FET)复苏周期妊娠率约为 48.71%^[17]。尽管我国辅助生殖技术快速发展,服务能力逐年提高,已有大量不孕不育家庭受益,仍应注意,即使达到近 50%的临床妊娠率,也意味着有一半的移植周期失败^[18]。

如何进一步提高辅助生殖助孕的成功率,不仅仰赖相关临床和基础科研的发展,也对临床工作各个流程的各个细节提出更高的挑战。

超声引导胚胎移植有经腹超声引导和经阴道超声引导两种途径^[19-21]。其中,经腹超声引导胚胎移植是较为经典的方式^[22],在我国大部分中心均开展此种方式引导移植;日本、欧洲等国家,国内亦有少数中心开展经阴道超声引导的胚胎移植^[23]。另一方面,国内也有部分中心采用无超声引导的胚胎移植方式,此类移植方式可能对移植者的技术和经验水平要求更高^[24]。虽然超声引导下的胚胎移植对 IVF 成功率的影响仍有部分争议,但就目前已有的研究结果而言,超声引导与体外受精结局

成正相关^[25],因此优化胚胎移植过程中的超声监测细节仍有积极的意义。之前已有研究证明指导憋尿可减少经腹妇科超声患者的不适体验,确保膀胱的适度充盈^[26]。本研究以此为出发点,通过随机、对照的方式,比较了移植前一天提前指导患者饮水量及憋尿方法以达到移植当日较理想的膀胱尿量这一方法对胚胎移植结局的影响。

本研究结果显示,提前指导憋尿对总妊娠率和35岁以上患者的移植妊娠率并无显著影响,但可以明显提高35岁以下年龄段患者的移植妊娠率($P<0.05$)。这一结果可能与年轻患者受教育水平和依从性更高有关,可以更严格准确地按照指导憋尿的步骤提前准备,在移植时达到膀胱适度充盈,从而在更清楚明确的超声引导下顺利移植的过程中受益。同时多项研究均证实,35岁以下的患者胚胎质量优于35岁以上的高龄患者^[27,28]。虽然本研究中纳入患者的移植胚胎均为优质胚胎,但35岁以上患者的卵母细胞染色体异常率以及胚胎染色体非整倍体率等影响妊娠率的因素明显较35岁以下患者更高。在本研究结果中也可以看到35岁以下患者的妊娠率高于35岁以上患者。在35岁以上患者移植前指导憋尿对妊娠率无明显影响,可能与该年龄段患者胚胎染色体异常率较高等因素相关,同时也存在移植质量更好胚胎的患者能够在移植前指导憋尿中获益更大这一可能性。

随着“二孩政策”的全面放开,生殖医学中心迎来大量具有前次剖宫产史、瘢痕子宫的患者。子宫下段剖宫产由耻骨联合上水平切口进腹后,需上推膀胱分离暴露子宫下段,部分剖宫产后患者存在膀胱粘连子宫这一并发症。本研究发现提前指导憋尿对瘢痕子宫和无子宫手术史患者移植结局无显著影响,但是,瘢痕子宫患者移植后的妊娠率均较无子宫手术史患者更高,造成这一差异的原因目前尚不明确。鉴于纳入对照组和指导组的瘢痕子宫患者数量较少(对照组10例,指导组11例),我们仍需要在下一步研究中纳入更多的具有子宫手术史的患者进行统计研究,以进一步探明提前指导憋尿对瘢痕子宫胚胎移植是否有积极意义。

综上所述,在小于35岁患者中,提前指导憋尿可明显改善移植妊娠率,但在瘢痕子宫和无子宫手术史的患者中,提前指导憋尿对移植妊娠率无明显影响。本研究样本量有限,这一结果仍需在更大样本量的随机对照研究验证;同时,如何提高35岁以上大龄不孕患者胚胎移植的成功率仍需进一步研究。

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