辅酶 Q10 联合金凤丸对体外授精 - 胚胎移植患者卵巢功能及子宫内膜容受性的影响 *

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摘要 目的:探讨辅酶 Q10 联合金凤丸对体外授精 - 胚胎移植患者卵巢功能及子宫内膜容受性的影响。方法:选择 2017 年 7 月~ 2017 年 10 月接诊的 185 例体外授精 - 胚胎移植患者进行研究,通过随机数表法将其分为观察组(n=95)和对照组(n=90)。对照组采用金凤丸进行治疗,观察组在对照组的基础上加用辅酶 Q10 进行治疗。治疗后,比较两组血清卵泡刺激素(FSH)、促黄体生成素(LH)、睾酮(T)、雌二醇(E_2)、胰岛素(INS)、子宫内膜厚度、孕激素(P)水平、获卵数、受精率及妊娠率。结果:治疗后,两组患者血清 FSH、LH、T、E_2、INS 水平均较治疗前明显下降,且观察组以上指标水平显著低于对照组($P<0.05$);两组患者子宫内膜厚度和血清 P 水平均较治疗前明显升高,且观察组以上指标均显著高于对照组($P<0.05$);两组患者获卵数无明显差异,观察组患者受精率、妊娠率均显著高于对照组($P<0.05$)。结论:辅酶 Q10 联合金凤丸可明显增加子宫内膜厚度,提高妊娠率。

关键词:辅酶 Q10;金凤丸;体外授精;胚胎移植;卵巢功能;子宫内膜容受性
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Effects of Coenzyme Q10 Combined with Jinfeng Pill on the Ovarian Function and Endometrial Receptivity of Patients Undergoing in VitroInsemination and Embryo Transfer*

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ABSTRACT Objective: To study the effects of coenzyme Q10 combined with jinfeng pill on the ovarian function and endometrial receptivity of patients undergoing in vitro insemination and embryo transfer. **Methods:** 185 cases of in vitro fertilization-embryo transfer patients who were treated from July 2017 to October 2017 were selected and divided into the observation group (n=95) and the control group (n=90) by the random number table method. The control group was treated with jinfeng pill, and the observation group was treated with coenzyme Q10 on the basis of the control group. After treatment, the serum follicle stimulating hormone (FSH), luteinizing hormone (LH), testosterone (T), estradiol (E_2), insulin (INS), endometrium thickness, progesterone (P) level, number of eggs obtained, fertilization rate and pregnancy rate were compared between the two groups. **Results:** After treatment, the serum levels of FSH, LH, T, E_2 and INS in the two groups were significantly lower than those before treatment, and the above index in the observation group were significantly lower than those in the control group ($P<0.05$). The endometrial thickness and serum P level in both groups were significantly higher than before treatment, and the above indicators in the observation group were significantly higher than those in the control group ($P < 0.05$). There was no significant difference in the number of eggs obtained between the two groups, and the fertilization rate and pregnancy rate of the observation group were significantly higher than those of the control group ($P<0.05$). **Conclusion:** Coenzyme Q10 combined with jinfeng pill can significantly increase the endometrial thickness and pregnancy rate.

Key words: Coenzyme Q10. Jinfeng pill; In vitro fertilization; Embryo transfer; Ovarian function; Endometrial receptivity
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前言

随着社会的发展,人们的工作压力增大,不孕不育的发病率也在逐年升高。体外授精 - 胚胎移植也叫试管婴儿,是一种人工生育技术,给不孕不育患者带来了福音。随着其迅速的发展,成功率不断升高,但是仍有超过半数患者在首次体外授精 - 胚胎移植中未成功受孕[1,2]。中医治疗不孕症历史悠久,体外授精 - 胚胎移植联合中医治疗能提高成功率。金凤丸具有温肾益

阳、调经助孕之功,但是目前对于其在生殖方面的应用效果仍不完全明确[3,4]。辅酶 Q10 是一种强抗氧化剂,是细胞自身产生的天然抗氧化剂和细胞代谢启动剂,可保护和恢复生物膜结构的完整性,使细胞免受自由基的破坏,改善患者子宫内膜的容受性[5,6]。但是,目前临床上对于两种药物联合治疗体外授精 - 胚胎移植的报道较少,本研究主要探讨了辅酶 Q10 联合金凤丸对体外授精 - 胚胎移植患者卵巢功能及子宫内膜容受性的影响,旨在为临床提供参考依据,结果报道如下。

1 资料与方法

1.1 一般资料

选择 2017 年 7 月～2017 年 10 月接诊的 185 例体外授精 - 胚胎移植患者进行研究。通过随机数表法分为两组,两组一般资料比较无显著差异($P>0.05$),具有可比性,详见表 1。所有患者均知情同意此研究,并签署知情同意书。纳入标准:(1)确诊为不孕的孕龄期妇女;(2)生殖内分泌激素在降调节后的"去势"水平;(3)抗苗勒氏管激素 ≤ 1.5 ng/mL。排除标准:① 生殖器畸形;② 男性原因导致不孕者;③ 精神异常,沟通障碍者。

1.2 治疗方法

对照组患者在前一月经周期给予金凤丸 (规格每 10 丸重 1.8 g,厂家:同溢堂药业有限公司,国药准字 Z20064400)1.8 g/次,1d 2 次。经期停用,服用 3 个经期。观察组在对照组的基础上加用辅酶 Q10(规格 10 mg,厂家:上海信谊药厂有限公司,国药准字 HH19999132)10 mg/ 次,1d 3 次。

表 1 两组患者一般临床资料比较($\bar{x}\pm s$)

Table 1 Comparison of the general clinical data between the two groups($\bar{x}\pm s$)

Groups	n	Age (years)	Infertility years (years)	The body of the quality(kg/m^2)
Observation group	95	32.27± 3.47	6.53± 3.87	21.43± 2.38
The control group	90	32.41± 2.69	6.78± 3.54	21.67± 2.24
t value		0.306	0.458	0.705
P value		0.760	0.648	0.482

1.3 观察指标

于治疗前及治疗后,采集清晨空腹血 8 mL,室温下静置 1h 后,以 3000 r·min^{-1} 离心 15 min 后,提取上层血清,置于冷冻箱内储存以备检测,血清 FSH、LH、T、E$_2$、INS 的测定均采用双抗体夹心酶联免疫吸附法(ELISA),试剂盒购于深圳晶美生物工程有限公司,所有操作均严格按照仪器及试剂盒说明书进行;采用多普勒超声诊断仪测定子宫内膜厚度;观察记录患者获卵率、受精率及妊娠率。

1.4 统计学分析

以 spss18.0 软件包处理数据,计量资料均为正态分布,以均数± 标准差($\bar{x}\pm s$)表示,组间比较使用独立样本 t 检验,计数资料以率表示,组间比较采用 x^2 检验,以 $P<0.05$ 表示差异具有统计学意义。

2 结果

2.1 两组患者治疗前后卵巢功能的比较

两组患者治疗前卵巢功能各指标水平比较无明显差异($P>0.05$);治疗后,两组患者血清 FSH、LH、T、E$_2$、INS 水平均较治疗前明显下降,且观察组以上指标均显著低于对照组($P<0.05$),见表 2。

表 2 两组患者治疗前后卵巢功能各指标水平的比较($\bar{x}\pm s$)

Table 2 Comparison of the levels of ovarian function before and after treatment between the two groups($\bar{x}\pm s$)

Groups	n	FSH(U/L)		LH(U/L)		T(ng/mL)		E$_2$(pg/mL)		INS(mU/L)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	95	5.63± 1.09	5.20± 0.68	10.39± 2.86	6.05± 1.62	72.14± 16.63	42.78± 12.31	50.92± 13.93	31.03± 7.99	19.13± 6.19	10.28± 3.92
Control group	90	5.60± 0.97	5.55± 0.95	10.62± 2.59	7.68± 2.15	71.55± 15.47	56.35± 11.38	51.78± 12.69	40.14± 9.35	18.78± 6.37	14.84± 4.73
t value		0.197	2.893	0.572	5.843	0.250	7.774	0.438	7.137	0.379	7.155
P value		0.844	0.004	0.568	0.000	0.803	0.000	0.662	0.000	0.705	0.000

2.2 两组患者治疗前后子宫内膜厚度和血清 P 水平的比较

两组患者治疗前子宫内膜厚度和血清 P 水平比较差异无统计学意义($P>0.05$);治疗后,两组患者子宫内膜厚度和 P 水平均较治疗前明显升高,且观察组以上指标均显著高于对照组($P<0.05$),见表 3。

2.3 两组患者受精率、临床妊娠率的比较

两组患者获卵数比较差异无明显统计学意义,观察组患者受精率、妊娠率均显著高于对照组($P<0.05$),见表 4。

3 讨论

随着国家二胎政策的全面放开,高龄助孕已成为全国各生殖中心不得不面对的一大课题、难题[7]。高龄患者卵巢储备功

表 3 两组患者治疗前后子宫内膜厚度和血清 P 水平的比较($\bar{x}\pm s$)

Table 3 Comparison of the endometrial thickness andserum P level between the two groups before and after treatment($\bar{x}\pm s$)

Groups	n	Intima thickness(mm)		P(μg/L)	
		Before treatment	After treatment	Before treatment	After treatment
Observation group	95	8.05± 1.83	12.53± 1.23	0.87± 0.39	1.41± 0.53
Control group	90	8.07± 1.85	11.32± 1.32	0.89± 0.41	1.01± 0.38
t value		0.074	6.454	0.198	5.871
P value		0.941	0.000	0.843	0.000

表 4 两组患者受精率、临床妊娠率的比较

Table 4 Comparison of the fertilization rate and clinical pregnancy rate between the two groups

Groups	n	Number of eggs (pieces)	Fertilization rate(%)	The pregnancy rate(%)
Observation group	95	13.62± 4.42	77(81.05)	53(55.79)
Control group	90	12.45± 5.06	64(71.11)	27(30.00)
statistics		1.677	2.520	12.524
P value		0.095	0.112	0.000

能、卵子质量及子宫内膜质量均有不同程度下降,助孕成功率低。改善高龄患者的卵巢储备、卵子质量、子宫内膜厚度及血流灌注等,可显著改善高龄不孕患者的妊娠结局[8,9]。

金凤丸是临床上治疗体外授精 - 胚胎移植的常用药,由淫羊藿、仙茅、益母草、阿胶、何首乌、肉桂、女贞子、鹿茸、人参组成,具有温肾益阳、调经助孕之功,但是其单一用药效果并不特别显著[10]。目前国内已有部分专家开始将辅酶 Q10 用于改善高龄不孕患者卵巢储备功能、卵子质量及子宫内膜容受性,且部分患者得到满意的妊娠结局[11,12]。辅酶 Q10 存在于线粒体内膜上,在生物体中能提供或移去氧,通过传递质子,维持线粒体膜电位,促进腺苷三磷酸[13,14]。

卵巢位于女性盆腔内, 主要功能是产生和排出卵细胞,分泌性激素,以促进女性性征的发育并维持之,且其大小形状随着年龄增长而改变,高龄患者卵巢储备功能有不同程度的下降[15,16]。有研究显示辅酶 Q10 对于高龄女性的卵母细胞线粒体具有一定的保护作用[17]。本研究结果显示治疗后,患者卵巢功能各指标水平有所下降,且联合辅酶 Q10 治疗的患者的血清 FSH、LH、T、E_2、INS 水平显著低于使用金凤丸治疗的患者,说明辅酶 Q10 能改善高龄不孕患者卵巢储备功能, 提高卵巢反应性,增加高龄助孕的成功率。分析是因为患者体内抗氧化物质通常是通过联合作用或者协同作用加强抗氧化效能,而辅酶 Q10 通过转换氧化还原性结构, 可阻止脂质及蛋白质的过氧化,清除体内和细胞的自由基,与金凤丸共同起到抗氧化作用,最终改善患者的卵巢功能。Angelova M A[18]研究结果显示辅酶 Q10 可改善体外授精 - 胚胎移植患者的卵巢储存功能,改变其妊娠结局。本研究结果也显示联合辅酶 Q10 治疗的患者的受精率、妊娠率均高于单独使用金凤丸治疗的患者, 提示辅酶 Q10 联合金凤丸可改善体外授精 - 胚胎移植患者卵巢储备功能,增加其成功率,使患者得到满意的妊娠结局。

子宫内膜容受性是指子宫内膜对胚胎的接受能力,是其接受胚胎着床的一种综合状态,这一时期被称为"着床窗口期",又称为种植窗,是胚胎着床的重要条件[19,20]。本研究结果显示联合辅酶 Q10 治疗的患者的子宫内膜厚度和血清 P 水平均显著高于使用金凤丸治疗的患者, 说明辅酶 Q10 联合金凤丸可有效改善体外授精 - 胚胎移植患者的子宫内膜容受性,提高其妊娠成功率。分析原因是因为辅酶 Q10 的生物活性主要来自于其醌环的氧化还原特性和其侧链的理化性质,是细胞自身产生的抗氧化和细胞代谢启动剂,能保护和恢复子宫内膜结构的完整性。

综上所述, 辅酶 Q10 联合金凤丸可明显增加子宫内膜厚度,提高妊娠率,而其具体机制还有待于进一步研究以明确。

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