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电针结合红外线照射对反复着床失败患者子宫内膜容受性、胚胎移植及妊娠情况的影响*

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摘要 目的:观察电针结合红外线照射对反复着床失败(RIF)患者子宫内膜容受性、胚胎移植及妊娠情况的影响。**方法:**选取 102 例于 2015 年 5 月-2018 年 5 月在我院行复苏胚胎移植的 RIF 患者,按照随机数字表法将患者分为电针结合红外线照射治疗组(A 组,38 例)、安慰针刺组(B 组,34 例)及空白对照组(C 组,30 例)。比较三组治疗前后血清雌二醇、孕酮水平,于治疗前后检测子宫内膜容受性超声学指标,包括子宫内膜厚度、内膜容积、血管血流指数(VFI)、内膜血流指数(FI)、阻力指数(RI),比较三组胚胎移植及妊娠情况。**结果:**三组治疗前后血清雌二醇、孕酮水平比较无统计学差异($P>0.05$)。治疗后 A 组子宫内膜厚度、内膜容积大于治疗前及 B 组、C 组,VFI、FI 高于治疗前及 B 组、C 组,RI 低于治疗前及 B 组、C 组($P<0.05$)。三组移植胚胎数、生化妊娠率、临床妊娠率比较无统计学差异($P>0.05$),A 组胚胎着床率高于 B 组、C 组($P<0.05$)。**结论:**电针结合红外线照射治疗 RIF 患者可以改善子宫内膜容受性,提高胚胎着床率。

关键词:电针;红外线照射;反复着床失败;子宫内膜容受性;妊娠

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Effect of Electro-acupuncture Combined with Infrared Irradiation on Endometrial Receptivity, Embryo Transfer and Pregnancy in Patients with Repeated Implantation Failure*

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ABSTRACT Objective: To observe the effect of electro-acupuncture combined with infrared irradiation on endometrial receptivity, embryo transfer and pregnancy in patients with repeated implantation failure (RIF). **Methods:** 102 RIF patients who underwent resuscitation embryo transfer in our hospital from May 2015 to May 2018 were selected. According to the random number table method, the patients were divided into electro-acupuncture combined with infrared irradiation treatment group (group A, 38 cases), placebo acupuncture group (group B, 34 cases) and blank control group (group C, 30 cases). The levels of serum estradiol and progesterone were compared before and after treatment among three groups, endometrial receptive ultrasound were measured before and after treatment, including endometrial thickness, endometrial volume, vascularization flow index (VFI), flow index (FI) resistance index (RI), embryo transfer and pregnancy were compared among three groups. **Results:** There was no significant difference in serum estradiol and progesterone levels among three groups before and after treatment ($P>0.05$). After treatment, the endometrial thickness, endometrial volume in group A were larger than those before treatment, group B and group C, VFI and FI were higher than those before treatment, group B and group C, RI was lower than those before treatment, group B and group C ($P<0.05$). There was no significant difference in the number of embryos transferred, biochemical pregnancy rate and clinical pregnancy rate among three groups ($P>0.05$), the implantation rate in group A was higher than that in group B and C ($P<0.05$). **Conclusion:** Electro-acupuncture combined with infrared irradiation can improve endometrial receptivity and embryo implantation rate in RIF patients.

Key words: Electro-acupuncture; Infrared irradiation; Repeated implantation failure; Endometrial receptivity; Pregnancy

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前言

随着辅助生殖技术不断进步,"试管婴儿"成功率也不断提高,但仍有部分患者发生反复着床失败(repeated implantation failure, RIF),即反复、连续移植3次或3次以上优质胚胎,或累计移植10个或10个以上优质胚胎后仍未孕,RIF发生率约为10%^[1,2]。胚胎着床的过程受多方面影响,且胚胎是否能成功着床及正常发育与患者的子宫内膜容受性、胚胎质量等息息相关。在每个月经周期中,人子宫内膜可接受胚胎植入仅4-5天,植入失败是女性不育的主要原因,而无法实现子宫内膜容受性是造成生殖技术失败的主要原因^[3-5]。因此,提高体外受精-胚胎移植(IVF-ET)妊娠率的关键,在于如何改善子宫内膜的受容性^[6]。针灸可以调整气血、活络经脉,对于不孕不育的治疗可以起到事半功倍的效果,而且因其易操作,见效快,价格低等特点被越来越多的国家和地区接受,最重要的是无任何毒副作用^[7,8]。国内外对针灸在辅助生殖技术中的作用进行了大量研究,多数研究认为针灸可以明显提高RIF患者的妊娠率和活产率^[9,10],但是其作用机制尚未完全阐明。近年来,红外线照射因其显著

的热效应带来的改善局部血运的特殊效果也被用于治疗阳痿、盆腔炎等不孕不育相关疾病^[11]。本研究针对RIF患者,选取适当穴位行电针结合红外线照射治疗,观察此类患者复苏胚胎移植周期子宫内膜各项指标、妊娠结局的变化,现报道如下。

1 资料与方法

1.1 一般资料

选取102例于2015年5月-2018年5月在我院行复苏胚胎移植的RIF患者,本研究经我院伦理委员会批注通过。患者纳入标准:(1)年龄<38岁;基础血卵泡刺激素(blood follicle stimulating hormone, bFSH)<15 U/L;(2)超声检查子宫形态基本正常;(3)移植3次或3次以上优质胚胎后仍未孕。排除标准:(1)彩超检查卵巢囊肿者;(2)高血压、糖尿病、甲状腺功能亢进等内分泌疾病者;(3)宫腔镜检查内膜病变者。按照随机数字表法将患者分为电针结合红外线照射治疗组(A组,38例)、安慰针刺组(B组,34例)及空白对照组(C组,30例),三组一般资料见表1,三组bFSH、不孕年限、年龄、不孕类型、体质量指数等比较无统计学差异($P>0.05$),均衡可比。

表1 三组一般资料比较

Table 1 Comparison of general data among three groups

Groups	Age(years old)	Infertility years (years)	Infertility Types[n(%)]		Body mass index (kg/m ²)	bFSH(U/L)
			Primary	Secondary		
Group A(n=38)	32.57± 4.25	6.11± 1.62	18(47.37)	20(52.63)	21.84± 0.77	7.34± 2.08
Group B(n=34)	33.71± 4.22	6.40± 1.31	16(47.06)	18(52.94)	21.49± 1.18	7.46± 1.63
Group C(n=30)	32.10± 4.54	5.30± 1.75	14(46.67)	16(53.33)	21.66± 0.78	7.43± 1.75
F	1.102	0.829		0.279	1.506	0.271
P	0.274	0.412		0.598	0.137	0.788

1.2 研究方法

子宫内膜准备:所有患者均使用激素人工周期法准备内膜:自月经第3天开始口服戊酸雌二醇6 mg/d,10天后超声观察子宫内膜情况,若厚度>8 mm,加用黄体酮转化内膜准备胚胎移植。若厚度<8 mm,继续使用戊酸雌二醇直至内膜>8 mm。
① 电针结合红外线照射治疗组(A组):针刺穴位取归来、子宫、血海、地机快速进针,行针,得气后,连接电极线,采用疏密波(2/80 赫兹),强度选择患者能耐受的最大舒适强度。电针治疗的同时,下腹部(包括归来、子宫穴等处)予以红外线照射,30 min/次,月经干净后开始实施,隔日1次,直至胚胎移植前1天。
② 安慰针刺组(B组):安慰针刺点为非经非穴部位,腹部安慰针刺点为肚脐下3寸,旁开3寸(双侧);下肢安慰针刺点为足三里穴和阳陵泉穴连线的中点(双侧)。尽量舒张皮肤,缓慢进针,浅刺<5 mm,无得气,不行针,连接电针,但电针保持在"虚拟模式",即无电流刺激状态。将红外线照射仪对着患者下腹部,但不打开电源。
③ 空白对照组(C组):不接受针刺及红外线治疗。

1.3 观察指标

于治疗前后抽取三组空腹静脉血5 mL,采用3000 r/min的转速离心10 min,提取上清液,采用放射免疫分析法检测血

清雌二醇、孕酮水平。于治疗前后检测子宫内膜容受性超声学指标,包括子宫内膜厚度、内膜容积、血管血流指数(vascularization flow index, VFI)、内膜血流指数(flow index, FI)、阻力指数(resistance index, RI)。比较三组胚胎移植及妊娠情况。

1.4 统计学方法

采用SPSS23.0进行统计分析,采用[n(%)]表示计数资料,实施 χ^2 检验,采用($\bar{x} \pm s$)表示计量资料,实施t检验,多组间比较采用F检验,检验水准 $\alpha=0.05$,以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 三组性激素水平比较

三组治疗前后血清雌二醇、孕酮水平比较无统计学差异($P>0.05$),见表2。

2.2 三组子宫内膜容受性比较

三组治疗前内膜容积、子宫内膜厚度、VFI、FI、RI比较无统计学差异($P>0.05$),治疗后A组子宫内膜厚度、内膜容积大于治疗前及B组、C组,VFI、FI高于治疗前及B组、C组,RI低于治疗前及B组、C组($P<0.05$),见表3。

表 2 三组性激素水平比较($\bar{x} \pm s$)Table 2 Comparison of sex hormone levels among three groups($\bar{x} \pm s$)

Groups	Estradiol(pg/mL)		Progesterone(ng/mL)	
	Before treatment	After treatment	Before treatment	After treatment
Group A(n=38)	241.58± 57.81	238.68± 43.73	0.96± 0.33	0.95± 0.32
GroupB(n=34)	234.88± 61.18	236.15± 51.78	1.09± 0.23	1.05± 0.27
Group C(n=30)	245.83± 56.27	243.57± 56.49	1.07± 0.30	1.07± 0.28
F	0.478	0.225	1.917	1.473
P	0.634	0.823	0.083	0.141

表 3 三组子宫内膜容受性比较($\bar{x} \pm s$)Table 3 Comparison of endometrial receptive among three groups($\bar{x} \pm s$)

Groups	Endometrial thickness (mm)		Endometrial volume(mL)		VFI		FI		RI	
	Before	After	Before	After	Before	After	Before	After	Before	After
	treatment	treatment	treatment	treatment	treatment	treatment	treatment	treatment	treatment	treatment
Group A (n=38)	9.01± 1.54	11.12± 1.56*	3.68± 1.07	5.14± 1.31*	1.65± 0.61	2.19± 0.74*	24.55± 6.05	28.72± 7.35*	0.62± 0.12	0.43± 0.11*
GroupB (n=34)	8.96± 0.92	9.41± 1.14 [#]	3.65± 0.84	3.77± 1.03 [#]	1.71± 0.49	1.73± 0.56 [#]	24.32± 5.34	24.16± 5.07 [#]	0.63± 0.17	0.61± 0.09 [#]
Group C (n=30)	8.83± 1.17	9.18± 1.21 [#]	3.59± 0.81	3.72± 0.88 [#]	1.54± 0.67	1.61± 0.71 [#]	23.64± 4.29	24.44± 4.61 [#]	0.59± 0.13	0.58± 0.08 [#]
F	0.165	5.769	0.131	5.201	1.475	4.002	0.172	3.085	0.291	5.523
P	0.871	0.000	0.896	0.000	0.145	0.000	0.865	0.000	0.772	0.000

Note: Compared with before treatment, * $P<0.05$; Compared with group A, [#] $P<0.05$.

2.3 三组胚胎移植及妊娠情况比较

差异($P>0.05$), A 组胚胎着床率高于 B 组、C 组($P<0.05$), 见表4。

三组移植胚胎数、生化妊娠率、临床妊娠率比较无统计学

表 4 三组胚胎移植及妊娠情况比较

Table 4 Comparison of embryo transfer and pregnancy among three groups

Groups	Number of embryos transferred(n)	Implantation rate[n(%)]	Biochemical pregnancy rate	Clinical pregnancy rate
			[n(%)]	[n(%)]
Group A(n=38)	1.78± 0.41	18(47.37)	19(50.00)	14(36.84)
GroupB(n=34)	1.89± 0.32	8(23.53) [#]	10(29.41)	6(17.65)
Group C(n=30)	1.77± 0.43	6(20.00) [#]	9(30.00)	5(16.67)
F	1.258	4.421	3.162	3.269
P	0.212	0.036	0.075	0.069

Note: Compared with group A, [#] $P<0.05$.

3 讨论

胚胎着床是一个多系统协作、极为复杂的生理过程,受到内分泌、免疫、生殖等多系统共同影响^[12,13]。子宫内膜容受性是指内膜允许囊胚粘附、穿透并植入而使胚胎着床的能力,此时也称为“植入窗口期”或“种植窗期”,子宫内膜的容受性依赖于胚胎与子宫内膜的同步发育,同时包含了多种复杂的调控机制,只有这些方面因素均已具备,囊胚才能顺利的着床生长^[14-16]。对于子宫内膜容受性影响比较大的是子宫内膜厚度,评价子宫内膜容受性的指标包括子宫内膜细胞形态学的胞饮突,分子生物学指标如血管上皮生长因子、白血病抑制因子、整合素家族等,超声学中的内膜厚度、形态、内膜下血流,以及血清

雌二醇和孕酮水平等^[17,18]。本研究选取拥有优质胚胎的 RIF 患者的复苏移植周期,排除了胚胎及外源性激素的影响,从而针对子宫内膜容受性的改变来评价电针结合红外线照射的治疗价值。

较高的动脉血流阻抗影响局部组织血供必定会造成子宫内膜容受性的下降,给予电针及红外线干预后治疗组的患者较其他两组患者,以及较自身治疗前在子宫内膜的厚度、子宫内膜的血流是显著提高的,而动脉血流阻力是显著降低的,因此我们考虑电针可以通过机械刺激、电流改善盆腔微环境,增加子宫内膜血供、减轻子宫动脉阻抗^[19]。针刺可改善胞饮突的生长发育情况,促进整合素分子表达,从而达到提高临床妊娠率、提高子宫内膜容受性、改善子宫微环境的作用^[20,21]。且有研究^[22]

将针灸对子宫内膜容受性的影响与其它治疗方法作比较,结果证明单一针灸治疗或联合其他治疗方法对子宫内膜容受性有较好的改善作用,因其相对于中西药物及西医其他相关治疗来说,对机体有整体调节作用。

从中医辩证角度看,患者主要因为痰实、血淤、肾虚、血虚等导致内膜容受性较差,以虚为主,虚实交杂,所以中医治疗原则是活血化瘀、补肾养血、调经冲任^[23,24],这与西医子宫内膜下血流异常造成的子宫内膜容受性下降理论不谋而合。本研究以此理论为依据进行穴位选择:归来穴有活血化瘀,调经止痛,条血室,温下焦的作用;子宫穴有调经理气,升提下陷之功效;血海穴有化血为气,运化脾血,调经统血,健脾化湿之功效;地机穴对女性来说主要有健脾、调经之用,以上穴位配伍在移植前可以起到活血通络,增加子宫内膜容受性的功效^[25,26]。关于针刺治疗的安全性,Xu Z^[27]等人的研究证实针刺在体外受精过程中并不会影响母婴结局,如妊娠期糖尿病,妊娠期高血压,胎盘植入等。

此外,本研究还辅助红外线照射治疗,红外线具有非常显著的热效应,当身体局部受到红外线照射时,细胞分子运动加速,局部温度升高,可带来血管扩张、血流加速、改善局部组织的营养、代谢和血供的特殊效应^[28-30]。红外线照射结合电针疗法,同时从中西医的角度对女性整体的生殖功能以及子宫局部环境进行良性影响,结果显示治疗后患者的子宫内膜厚度、子宫内膜容积、子宫血流指数显著提高,动脉阻抗显著降低,胚胎着床率显著升高。虽然治疗干预后生化妊娠率、临床妊娠率改善并无统计学差异,但较未干预者明显升高,后期研究病例增加后这种趋势将更显著,需做进一步研究探讨。

综上所述,电针结合红外线照射治疗 RIF 患者可以改善子宫内膜容受性,提高胚胎着床率。

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