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补肾调经汤联合 B 超对卵巢储备功能不良患者辅助生殖技术中 胚胎质量的影响*

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摘要 目的:探讨与分析补肾调经汤联合 B 超对卵巢储备功能不良(DOR)患者辅助生殖技术中胚胎质量的影响。**方法:**选择 2018 年 8 月到 2021 年 1 月在本院就诊的 58 例卵巢储备功能减退不孕患者作为研究对象,根据 1:1 随机分配原则把患者分为汤药组与对照组各 29 例。对照组给予戊酸雌二醇片联合地屈孕酮片治疗,汤药组在对照组治疗的基础上给予补肾调经汤口服治疗,治疗观察 3 个月经周期。**结果:**治疗后汤药组的总有效率 96.6%,高于对照组的 75.9% ($P<0.05$),所有患者在治疗期间无出现不良反应情况。两组治疗后的血清促黄体生成素(LH)、雌二醇(E2)含量低于治疗前,汤药组低于对照组 ($P<0.05$)。两组治疗后的卵巢动脉收缩期峰值流速(PSV)与卵巢动脉舒张末期流速(EDV)都高于治疗前,汤药组高于对照组 ($P<0.05$)。两组治疗后的窦状卵泡数高于治疗前,汤药组高于对照组 ($P<0.05$)。所有患者治疗后随访 1 年,汤药组的 1 年妊娠率为 72.4%,高于对照组的 27.6% ($P<0.05$)。**结论:**补肾调经汤在卵巢储备功能不良患者的应用能促进提高 B 超窦状卵泡数,提高卵巢动脉的血流速度,有利于性激素分泌正常,可提高胚胎质量,发挥整体治疗效果,有利于促进患者妊娠。

关键词:补肾调经汤;卵巢储备功能不良;B 超

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Effects of Bushen Tiaojing Decoction Combined with B-ultrasound on Embryo Quality in Assisted Reproductive Technology in Patients with Decreased Ovarian Reserve*

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ABSTRACT Objective: To explore and analysis the effects of Bushen Tiaojing Decoction combined with B-ultrasound on embryo quality in assisted reproductive technology in patients with decreased ovarian reserve (DOR). **Methods:** From August 2018 to January 2021, A total of 58 cases of infertile patients with reduced ovarian reserve who were treated in our hospital were selected as the research subjects, and the patients were divided into the decoction group and the matched group with 29 patients in each group accorded to the 1:1 random allocation principle. The matched group were given estradiol valerate tablets combined with dydrogesterone tablets for treatment, the decoction group were given the oral treatment of Bushen Tiaojing Decoction on the basis of the treatment of the matched group, and the treatment were observed for 3 menstrual cycles. **Results:** After treatment, the total effective rates of the decoction group were 96.6%, which were higher than that of the matched group of 75.9% ($P<0.05$). All patients had no adverse reactions during the treatment period. The levels of serum luteinizing hormone (LH) and estradiol (E2) in the two groups after treatment were lower than those before treatment, and those in the decoction group were lower than those in the matched group ($P<0.05$). The peak systolic velocity (PSV) and end-diastolic flow velocity (EDV) of ovarian artery in both groups after treatment were higher than those before treatment, and the decoction group were higher than the matched group ($P<0.05$). The number of antral follicles in the two groups after treatment were higher than that before treatment, and the decoction group were higher than that in the matched group ($P<0.05$). All patients were followed up for 1 year after treatment, the 1-year pregnancy rate in the decoction group were 72.4%, which were higher than that in the matched group (27.6%) ($P<0.05$). **Conclusion:** The application of Bushen Tiaojing decoction in patients with poor ovarian reserve function can promote the number of sinus follicles of B-ultrasound, improve the blood flow rate of ovarian artery, facilitate the normal secretion of sex hor-

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mones, improve the quality of embryos, exert the overall therapeutic effect, and facilitate the pregnancy of patients.

Key words: Bushen Tiaojing Decoction; Decreased ovarian reserve; B-ultrasound

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前言

卵巢储备功能不良(Decreased ovarian reserve, DOR)是指卵巢皮质区内卵泡生长、发育并形成可受精卵泡的能力减弱,使得原始卵泡数量异常下降或过早下降而导致的一类疾病^[1]。卵巢储备功能不良会对患者生育能力产生严重影响,减少患者月经量,且月经周期出现紊乱,是当前导致女性不孕的重要原因之一,可严重影响患者的身心健康^[2]。卵巢储备功能不良患者若不加干预,可造成病情进展,多数患者可发展到卵巢早衰。卵巢储备功能不良的发病隐匿,研究发现其发病机制与病因均较为复杂,当前西医暂无高效治疗方案,临床治疗以激素替代为主,通过诱导建立周期性的月经,促进月经规律恢复^[3,4]。但长期使用激素会导致患者病情反复发作,可能会引发激素依赖性肿瘤疾病,存在比较多的不良反应^[5]。传统中医并无卵巢储备功能不良相对应的疾病名称,但是可归为“不孕”、“经水不通”、“月经过少”、“经水不通”等范畴,其发病与肝气郁结、肾血不足有关,在治疗上需要疏肝解郁、滋阴补肾^[6,7]。补肾调经汤具有活血养血、滋养肾气、疏肝理气等功效,正符合卵巢储备功能不良的辨证施治原则^[8]。随着影像学技术的发展,B超的快速、准确及可重复性等优势得到了广泛认可,特别是B超可反映卵巢

储备功能,卵巢储备功能也具有很好的预测价值^[9]。本文具体探讨与分析了补肾调经汤联合B超对卵巢储备功能不良患者辅助生殖技术中胚胎质量的影响,以促进补肾调经汤的应用。现报道如下。

1 资料与方法

1.1 研究对象

选择2018年8月到2021年1月在本院就诊的58例卵巢储备功能减退不孕患者作为研究对象。

纳入标准:符合卵巢储备功能减退的诊断标准;不孕年限 ≥ 2 年;已婚,有正常性生活;入院前3个月未使用激素类药物;患者自愿参加临床研究;医院伦理委员会批准了此次研究。

排除标准:生殖器官结构异常者;合并先天性生殖器官发育不良者;存在卵巢切除史的患者;多囊卵巢综合征、输卵管疾病、垂体肿瘤患者;对研究药物过敏者;临床资料缺乏者;因男性因素导致不孕者;合并认知功能障碍或精神异常者;小学及其以下文化者。

根据1:1随机分配原则把患者分为汤药组与对照组各29例,两组患者一般资料对比无差异($P>0.05$)。见表1。

表1 一般资料对比

Table 1 Comparison of general data between the two groups

Groups	n	Body mass index (kg/m ²)	Years of infertility (years)	Age (years)	Years of education (years)	Blood sugar (tendency/L)	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)
Decoction group	29	22.11 $\pm$ 1.67	3.52 $\pm$ 0.25	33.24 $\pm$ 3.06	15.83 $\pm$ 2.84	5.76 $\pm$ 0.22	128.29 $\pm$ 11.17	76.38 $\pm$ 3.16
Matched group	29	21.16 $\pm$ 1.45	3.51 $\pm$ 0.33	33.10 $\pm$ 2.17	15.67 $\pm$ 3.29	5.77 $\pm$ 0.18	129.00 $\pm$ 10.47	76.39 $\pm$ 2.17

1.2 治疗方法

对照组:给予戊酸雌二醇片联合地屈孕酮片治疗,于月经后5d服用戊酸雌二醇片(国药准字H20000031,北京协和药厂),1mg/次,1次/d。于月经16d后服用地屈孕酮片(国药准字H20090470,荷兰Solvay Pharmaceuticals B.V.公司),10mg/次,1次/d,治疗观察3个月经周期。

汤药组:以对照组治疗为基础,给予补肾调经汤口服治疗,组方:菟丝子20克、山药20克、炙黄芪15克、白芍15克、补骨脂15克、当归15克、益母草15克、山茱萸10克、丹参10克、熟地黄10克、川芎10克、香附10克、甘草10克。水煎300mL,于早晚两次温服,月经期停药,也治疗观察3个月经周期。

1.3 观察指标

1.3.1 疗效标准 (治愈+显效)/组内例数 $\times 100.0\%$ =总有效率。治愈:月经周期、经期、经量恢复正常,显效:经量过多者相较治疗前减少1/3,月经周期恢复至 28 ± 7 d;有效:月经周期、经期相较治疗前稍有改善,无效:月经周期、经期相较治疗

前均无改善甚或恶化。

1.3.2 LH、E2含量检测 在治疗前后抽取2-3mL患者空腹静脉血,在分离血清后,黄体生成素(Luteinizing hormone, LH)、雌二醇(Estradiol, E2)含量通过电化学发光法进行检测。

1.3.3 B超检测 所有患者在治疗前后进行B超检测,使用Voluson E8阴道探头进行双侧卵巢扫描,获得整个卵巢图像,采用自动容积计算软件自动获得卵巢内所有窦卵泡数。同时测量与记录卵巢动脉收缩期峰值流速(Peak systolic velocity, PSV)与卵巢动脉舒张末期流速(End-diastolic flow velocity, EDV),连续测量3次,并取平均值作为结果。

1.3.4 成功妊娠率统计 所有患者在治疗后随访1年,统计患者的成功妊娠率,包括妊娠、分娩等。

1.4 统计方法

本次研究统计软件为SPSS24.00,检验水准为 $\alpha=0.05$ 。计量数据与计数数据均以均数 $\pm$ 标准差、n%等表示,对比为卡方 χ^2 检验分析与t检验分析, $P<0.05$ 为差异具有统计学意义。

2 结果

治疗后汤药组总有效率为 96.6 %，高于对照组的 75.9 % ($P<0.05$)，所有患者在治疗期间无出现不良反应情况。见表 2。

2.1 总有效率对比

表 2 总有效率对比(n)

Table 2 Comparison of total effective rate after treatment (n)

Groups	n	Cure	Excellent	Valid	Invalid	Total effective rate
Decoction group	29	24	4	1	0	28(96.6 %) [#]
Matched group	29	18	4	4	3	22(75.9 %)

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

2.2 血清性激素变化对比

于对照组($P<0.05$)。见表 3。

两组治疗后的血清 E2 与 LH 含量低于治疗前，汤药组低

表 3 血清性激素变化对比(均数± 标准差)

Table 3 Comparison of serum sex hormone changes (mean ± standard deviation)

Groups	n	E2(ng/L)		LH(U/L)	
		Pretherapy	Post-treatment	Pretherapy	Post-treatment
Decoction group	29	54.63± 5.39	31.58± 3.18 ^{**}	4.09± 0.35	2.32± 0.15 ^{**}
Matched group	29	54.77± 4.18	36.09± 4.44 [*]	4.11± 0.25	3.11± 0.24 [*]

Note: Compared with matched group, [#] $P<0.05$; Compared with pretherapy, ^{*} $P<0.05$, the same below.

2.3 卵巢动脉血流速度变化对比

组高于对照组($P<0.05$)。见表 4。

两组治疗后的卵巢动脉 PSV 与 EDV 都高于治疗前，汤药

表 4 卵巢动脉血流速度变化对比(cm/s, 均数± 标准差)

Table 4 Comparison of changes in ovarian arterial blood flow velocity (CM /s, mean ± standard deviation)

Groups	n	PSV		EDV	
		Pretherapy	Post-treatment	Pretherapy	Post-treatment
Decoction group	29	8.22± 0.18	13.29± 1.11 ^{**}	1.87± 0.24	3.94± 0.35 ^{**}
Matched group	29	8.21± 0.27	10.89± 0.82 [*]	1.88± 0.21	2.67± 0.16 [*]

2.4 窦状卵泡数变化对比

($P<0.05$)。见表 5。

两组治疗后的窦状卵泡数较治疗前高，汤药组较对照组高

表 5 窦状卵泡数变化对比(个, 均数± 标准差)

Table 5 Comparison of the number of sinus follicles (mean ± standard deviation)

Groups	n	Pretherapy	Post-treatment
Decoction group	29	4.05± 0.24	7.45± 0.28 ^{**}
Matched group	29	4.06± 0.33	5.43± 0.17 [*]

2.5 1 年妊娠率对比

所有患者治疗后随访 1 年，汤药组的 1 年妊娠率为 72.4 %，高于对照组的 27.6 %($P<0.05$)。

3 讨论

当前卵巢储备功能不良的病因比较复杂，可能与自身免疫代谢因素、医源性因素、遗传因素等存在相关性^[10]。很多卵巢储

备功能不良患者可因生殖能力出现提前衰退，因此在临床上会表现为与年龄不符的围绝经期症状，主要表现为月经过少、月经紊乱等^[1]。中医记载卵巢储备功能不良则以脾虚、痰湿为主要病机。中医认为，“肥白人多痰湿”，“脾为生痰之源”，“诸湿肿满，皆属于脾”。卵子排出依赖于肾阳的鼓动作用，卵子是肾所藏之“阴精”，肾阳亏虚，不能鼓舞肾阴滋育^[12]。目前临床上多采用雌激素类药物改善患者卵巢功能，虽然有一定的近期疗

效,但是很难持续改善患者预后,且长期使用可让患者产生药物抵抗性,患者用药依从性较差^[13,14]。中医药治疗卵巢储备功能不良具有较长的研究史,治疗以整体观念、辨证论治为指导,能够增强卵巢对促性腺激素的反应力,可对患者的下丘脑-垂体-卵巢轴功能进行整体调控,促进卵巢功能改善或恢复^[15]。本研究显示治疗后汤药组的总有效率96.6%,高于对照组的75.9%,所有患者在治疗期间无出现不良反应情况;所有患者治疗后随访1年,汤药组的1年妊娠率为72.4%,高于对照组的27.6%。该结果与陈博等人^[16]的报道具有一致性。分析可知:在补肾调经汤中,菟丝子、山药、炙黄芪可温壮肾阳、调理冲任、滋阴填精、温补督脉;白芍、补骨脂、当归可补肝养血、活血行气、中开郁结、下调经水;益母草、山茱萸、丹参可补益真阴且利血脉,还可滋肾阴,与熟地黄、川芎、香附、甘草合用而温阳补血解郁,调理冲任,从而发挥整体治疗效果,有利于促进患者妊娠,提高胚胎质量^[17,18]。

卵巢储备功能不良患者常伴有下丘脑-垂体-性腺轴功能衰退,还可在临床上表现为E2与LH升高^[19,20]。特别是当卵巢功能减退时,卵巢分泌功能有所下降,且导致垂体大量分泌促性腺激素,进而大量表达E2与LH^[21]。本研究显示两组治疗后的血清E2与LH含量低于治疗前,汤药组低于对照组。该结果与梁如碧等人^[22]的报道具有一致性。分析可知,中医认为卵巢储备功能不良患者多以肾虚肝郁证居多,肾虚为本病的病机基础,因此在治疗上需补肾疏肝。补肾调经汤具有强脾利湿之功效,可调节机体的胰岛素与葡萄糖代谢,可通过降低肝组织葡萄糖代谢酶水平而改善胰岛素抵抗,改善机体的子宫内膜容受性,从而有利于性激素分泌正常^[24]。

卵巢储备功能不良将会造成女性不孕,该类疾病患者的卵巢体积会明显减小,减少窦状卵泡数数量,降低卵巢反应性^[25,26]。激素替代疗法可缓解患者的临床症状,促进近期排卵,但是很难发挥促进持续排卵的作用^[27]。B超可以在短时间内动态测量和计算卵巢体积、卵泡数和卵巢基质血流,并可以对测量信息进行存储用于离体分析,还可检测基础窦卵泡数^[28]。两组治疗后的卵巢动脉PSV与EDV都高于治疗前,汤药组高于对照组;两组治疗后的窦状卵泡数高于治疗前,汤药组高于对照组,表明补肾调经汤在卵巢储备功能不良患者的应用能促进提高B超窦状卵泡数,提高卵巢动脉的血流速度。该结果与李文梅等人^[29]的报道具有相似性。分析可知,补肾调经汤从多个方面共同作用,共行疏肝解郁、滋阴补肾之功效,还可改善卵巢的血供,增加窦状卵泡数量^[30]。不过由于经费原因,本次研究的随访时间比较短,纳入患者数量比较少,没有进行辩证治疗探讨,将在后续研究中分析。

总之,补肾调经汤在卵巢储备功能不良患者的应用能促进提高B超窦状卵泡数,提高卵巢动脉的血流速度,有利于性激素分泌正常,可提高胚胎质量,发挥整体治疗效果,有利于促进患者妊娠。

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