

· 中医药 · 中西医结合 ·

连方教授“脾肾同治”在辅助生殖技术中的运用

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摘要: 介绍连方教授脾肾同治配合辅助生殖技术(ART)治疗不孕症的临床经验。针对多囊卵巢综合征不孕予二至天癸方合启宫丸加减治疗;子宫内膜异位症不孕者予祛瘀解毒方调理;高龄女性不孕者尤重经后三期辨证论治。临床施治,主张善用经方、活用药对。

关键词: 脾肾同治; 经方; 药对; 辅助生殖技术; 不孕症

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Application of Professor Lian Fang's "simultaneous treatment of spleen and kidney" in assisted reproductive technology

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Abstract: This paper introduces the clinical experience of Professor Lian Fang's simultaneous treatment of spleen and kidney combined with assisted reproductive technology (ART) in the treatment of infertility. For infertility patients with polycystic ovary syndrome, Erzhi Tianguai Recipe and Qigong Pills were treated with addition and subtraction; those with endometriosis were treated with Quyu Jiedu Recipe; Infertile women of advanced reproductive age should be pay special attention to the treatment of the three stages after menstruation. In clinical treatment, it is advocated to make good use of classical prescriptions and make active use of drug-pair.

Keywords: Simultaneous treatment of spleen and kidney; Classical prescriptions; Drug-pair; Assisted reproductive technology; Infertility

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脾肾同治始于《黄帝内经》,其后张仲景提出补益脾肾治疗大法,至李中梓重视先后天并调,脾肾同治理论逐渐完善并用于临床。陈修园认为“水与土相调,则草木生;脾与肾相合,则胎息成”^[1],是不孕症从脾肾论治的理论依据。连方教授是山东中医药大学附属医院生殖与遗传中心主任医师、博士研究生导师、岐黄学者、山东省名中医,开创了全国中医系统第一家获得卫生部批准开展人类辅助生殖技术(ART)的生殖与遗传中心,从事妇科临床、教学及科研工作数十载,擅长中西医结合诊治妇科诸疾,尤其在不孕症诊治方面造诣颇高,将脾肾同治理论灵活运用

于辅助生殖技术中,现将其经验介绍如下。

1 辨证审因,脾肾并调

“求子之道,莫如调经”,ART前3~6个月是畅通胞脉胞络、调理月经的重要时期。“调经之要,贵在补脾胃以资血之源,养肾气以安血之室”^[2],辨病与辨证相结合,针对病因病机,脾肾并调,恢复“肾-天癸-冲任-胞宫”轴正常功能。

1.1 滋肾运脾、祛瘀化湿调理多囊卵巢综合征(PCOS) PCOS患者常因排卵障碍而不孕。促性腺激素(Gn)诱导排卵,或行体外受精-胚胎移植(IVF-

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ET)可助其受孕。但PCOS患者卵泡数量多质量低,对Gn反应敏感,若大量募集卵泡发育可致卵巢过度刺激综合征(OHSS)。临床常小剂量促排药物联合滋肾运脾通利奇经,标本兼顾。PCOS以脾肾两虚为本,痰瘀为标。《素问·上古天真论》言:“女子二七而天癸至,任脉通,太冲脉盛,月事以时下,故有子”^[3]。肾精充沛,天癸化生,脾气健运,气血旺盛,蓄灌冲任,胞宫得养,才能行经孕育。正常的行经与排卵是受孕的先决条件,卵子属生殖之精,肾之阴精是卵子发育成熟的基础,冲任经脉气血和畅是排卵的必要条件^[4],若脾肾两虚,精血乏源,生殖之精难以泌至。脾肾共司水液代谢,两脏虚损,痰湿内生,“随气升降,无处不到”,壅阻冲任,致气滞血瘀,氤氲之时排卵障碍,可致不孕。治以二至天癸方合启宫丸加减(女贞子、旱莲草、枸杞子、菟丝子、当归、白芍、川芎、熟地黄、制香附、炙甘草、陈皮、制半夏、茯苓、苍术),补中有消,标本同治。二至天癸方为自拟经验方,由二至丸合四物汤加味组方,二至丸出自《医方集解》补益剂,方中女贞子甘苦凉,旱莲草甘酸寒,相须配伍滋补肝肾之效强,再入平补肝肾的枸杞子和菟丝子共为君药,补而不膩;女子不受胎者,气盛血衰,臣四物汤健脾养血,使精血化生,熟地大补真水,充养天癸,助君药滋肾阴;佐以“气中血药”香附理气调冲任,助四物补血和血;甘草调和诸药,固护阴血。全方补肾益阴,充养癸水,使生殖之精藏之足,乃能泄,藏泄正常,则经调子嗣^[5]。针对痰盛之标,用以二陈汤为基础的启宫丸,“身体过于肥盛,脂满子宫而不纳精,治用启宫丸,速效”^[1]。

1.2 补脾实肾,化痰解毒调治子宫内膜异位症(EMs) EMs是生育期妇女的常见病,30%~40%患者不孕^[6]。异位内膜侵袭力强,影响广泛,主张ART助孕与中医治疗相结合,整体调理,以期成功孕育。EMs以脾肾虚为本,瘀血为因。先天不足或后天失养,损伤脾肾机能,使冲任气血失和,胞宫藏泻失常,经血不循常道,行于胞宫之外,乃为瘀血,滞于胞脉,留于胞宫,则成癥瘕,可表现为“月经过多”、“崩漏”等症;不通则痛,故伴痛经且进行性加重;氤氲之时癥瘕阻碍两精相搏,难以摄精成孕。瘀血日久,郁而生热,热酿为毒,瘀毒互为因果,毒蕴又可加重血瘀^[7],病情缠绵难愈。《妇人规》云:“妇人久癥宿痞,脾肾必亏”,瘀毒不去,新血难生,中土失养,化精乏源,肾气失充,终成脾肾两虚兼血瘀的虚实错杂之证。自拟祛瘀解毒方(大血藤、玫瑰花、金银花、连翘、丹参、当归、白芍、川芎、生地、炙甘草等),大血藤、玫瑰花和

丹参意在祛瘀;银翘重在解毒,又透热转气^[8];四物汤易熟地为生地,凉血止血又补血活血,祛邪而不伤正;入黄芪、阿胶益气补脾,生精养血;肾虚者入仙灵脾、巴戟天;肾阴虚者加女贞子、墨旱莲。全方解毒散结以治标,补脾实肾以治本。痛经甚者酌加乌药、五灵脂以止痛,气滞明显者可加元胡、香附行血中之瘀滞,开经络之壅遏。

1.3 补肾固本、健脾养血调护高龄不孕 高龄不孕以肾虚为本,脾虚为要。年逾五七,阴精亏虚,天癸化生尤赖后天水谷滋养,但阳明脉衰,脾虚不能为胃行其津液,根弱源乏,血海不盈,月经后期、量少甚至闭经,生育能力急剧下降。ART联合周期疗法可在一定程度上改善高龄不孕患者卵巢储备及子宫内膜容受性,提高助孕成功率。周期疗法以补肾扶脾为基础,因时制宜,根据月经周期气血盈亏的变化酌加养血活血之品。经本阴血,出诸于肾,化生于脾,精血同源,精足可化血生血,血足亦可生精养精。经后期为肾阴及天癸滋长的重要时期,奠定了整个月经周期的物质基础,只有物质基础雄厚,方能恢复和提高月经周期演变的水平^[9]。经后常分三期论治,以滋肾填精的二至天癸方为基础,早期(月经周期第6~7天),阴精初长,加山药、当归等补脾养血之品,以阴扶阴;中期(月经周期第8~10天)为阴长的中期,阴中有阳,入白术、山萸肉等温补脾阳之品,以“阳中求阴”;晚期(月经周期第11~13天)阴长至极,加党参、黄芪等益气健脾之品,为氤氲之时的气血活动做准备。高龄闭经的患者,病程较长,ART术前雌孕激素序贯联合周期疗法3个月经周期。

2 遣方用药、明理知变

2.1 经方为主、灵活加减

2.1.1 桂枝茯苓丸 桂枝茯苓丸出自《金匮要略·妇人妊娠病脉证并治第二十》,方中桂枝辛温利血脉,茯苓甘平益脾,桃仁、丹皮活血化瘀,芍药养血和营,具祛瘀生新之效。常用于癥瘕不孕患者ART前预处理。下腹部所生结块影响胞宫,正虚邪入,阻滞气机,气滞血停,积而成瘀,乃为癥瘕。邪留不去,久病及肾,气血亏虚,致脾肾两虚兼血瘀的正虚邪实之证。《中藏经》言“真气失而邪气并”,故对于不孕合并子宫肌瘤、卵巢囊肿患者,常用桂枝茯苓丸补虚祛邪,攻补兼施,为ART创造良好的生殖内环境。此方可入女贞子、菟丝子补肾填精,加葛根、香附理气养血,调理冲任,于促排卵治疗中助卵泡成熟。扳机日应用桂枝茯苓丸可活血温经,畅通气血,外用淫羊藿、

杜仲、黄芪、丹参等益肾健脾之品熏洗足浴,补肾活血,内外兼治以触发排卵。

2.1.2 真武汤 真武汤为治疗脾肾阳虚、水气内停的方剂,出自《伤寒论》。水之制在脾,水之主在肾,辛甘性热的制附子为君药,温肾助阳,化气行水,兼暖脾土,温运水湿;臣以白术、茯苓健脾燥湿,泽泻利水渗湿,引湿邪从小便去;佐生姜、桂枝温散水湿;白芍利小便,又防附子燥热伤阴。促排中超过生理状态数目的卵泡被排出,可致 OHSS,肾精迅速丢失,阴损及阳,肾阳虚衰,水液气化失司,见小便不利;命门火衰,火不暖土,而纳呆便溏;湿停中焦,则为腹水;湿阻气机,则脘腹痞闷。此脾肾两虚为本,水饮停滞为标之阳虚水泛证,治以真武汤加减脾肾同调。邪留卵巢而体积增大明显者,常加牡蛎、皂刺软坚散结;面浮足肿,小便量少者,可入防己、黄芪利水消肿。

2.2 药对为先、巧妙组方

2.2.1 党参-菟丝子 甘平之党参,归脾肺经,气血双补,《本草正义》记载“党参能补脾养胃、健运中气”。菟丝子辛甘平,入脾肾肝三经,《内经》曰:“肾苦燥,急食辛以润之”,菟丝子之辛,“补而不峻”“守而能走”。两药合用平补脾肾,填精养血。连方以此药对组成参芪寿胎丸方,用于胚胎移植后的安胎养胎。“肾以载胎”,肾气不足则胎元失固,“胎茎系于脾”,胎儿生长发育赖气血的滋养。参芪寿胎丸方(菟丝子、桑寄生、盐续断、盐杜仲、党参、黄芪、白芍、麸炒白术等)中党参、菟丝子各 15 g,入脾肾以滋阴助阳,合寿胎丸立形体之基;臣以黄芪、白术益气生血,成形体之壮。如此,肾得补、血得养,自然胎长母安。腹痛者可倍白芍用量,合炙甘草缓急止痛;虚烦不眠者,加合欢花、炒枣仁养心解郁,安神养胎^[10]。

2.2.2 砂仁-续断 辛温之砂仁,归脾胃肾经,《本草纲目》言“补肺醒脾,养胃益肾,理元气,通滞气”,用治女子腹痛、崩中、胎动不安等疾。续断补肝肾,强筋骨,性微温,补而不滞,《本草汇言》称“所断之血脉非此不续……所损之胎孕非此不安”。两药相合,温中养胎,砂仁又可引气归肾,加强益肾安胎之效。合补气健脾之人参、白术,滋阴养血之熟地、当归,固肾益精之菟丝子、桑寄生,用于 IVF 反复种植失败之脾肾两虚证。

2.2.3 白术-覆盆子 白术苦甘,补气健脾,“守而不走”。覆盆子酸甘,滋补肝肾,“强阴健阳”,又“无燥热之偏”,“无疑涩之害”。两药相合,脾肾同治,固精益气,精充则化生有源,气固则血海自安。伍以枸杞

子、菟丝子,用于 ART 前调治脾肾两虚之月经失调及男子少、弱精症。

2.2.4 茯苓-菟丝子 茯苓甘淡,甘能补、淡能渗,归心肺脾肾经,《日华子本草》言其“补五劳七伤,安胎,暖腰膝,开心益智,止健忘”^[11]。菟丝子补脾肝肾,两药相合,直入脾肾经,温肾运脾,灵活组方,用于脾肾两虚兼痰湿之 PCOS、癥瘕等患者 ART 前预处理。

连方教授将脾肾同治与 ART 相结合,在调经助孕、诱发排卵、安胎养胎、防治术后并发症等方面,谨守病机,审因论治,补肾扶脾,先后天并调,使中医药与 ART 相辅相成,收效颇好。

参考文献

- [1] 林慧光.陈修园医学全书:明清名医全书大成[M].北京:中国中医药出版社,1999.
Lin HG.Chen Xiuyuan's Complete Book of Medicine:the Complete Book of famous doctors in the Ming and Qing Dynasties [M]. Beijing:China Press of Traditional Chinese Medicine,1999.
- [2] 张景岳.景岳全书[M].北京:人民卫生出版社,1959:75.
Zhang JY.The complete Book of Jingyue [M]. Beijing: People's Health Publishing House,1959:75.
- [3] 王冰.黄帝内经素问[M].南宁:广西科学技术出版社,2016.
Wang B.The Yellow Emperor's Classic of Medicine [M].Nanning: Guangxi Science and Technology Press,2016.
- [4] 许丽绵,罗颂平.排卵障碍的病机探讨[J].中国中医药信息杂志,2003,10(3):4-5.
Xu LM,Luo SP.Pathogenesis of ovulation disorder [J].Chin J Inf Tradit Chin Med,2003,10(3):4-5.
- [5] 连方,孙金龙,孙振高,等.二至天葵方对高龄妇女体外受精技术中优质胚胎率的影响[J].中国中西医结合杂志,2018,38(11):1306-1311.
Lian F,Sun JL,Sun ZG,et al.Effect of erzhi Tianguai recipe on high quality embryo rate and follicular fluid proteomics of elderly IVF women [J]. Chin J Integr Tradit West Med, 2018, 38 (11): 1306-1311.
- [6] 王曼.盆腔子宫内膜异位症与不孕[J].实用妇科与产科杂志,1987,3(4):177-178.
Wang M. Pelvic endometriosis and infertility [J]. Chin J Pract Gynecol Obst,1987,3 (4):177-178.
- [7] 连方.子宫内异位症病机——瘀毒学说[J].中国中西医结合杂志,2008,28(11):968-969.
Lian F. Stasis - toxin theory for pathogenesis of endometriosis [J]. Chin J Integr Tradit West Med,2008,28(11):968-969.
- [8] 戚敏,张建伟,李杰.连方教授治疗子宫内膜异位症经验[J].湖南中医杂志,2013,29(7):36-37.
Qi M,Zhang JW, Li J. Professor Lian Fang's experience in treating endometriosis [J]. Hunan J Tradit Chin Med,2013,29(7):36-37.

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参考文献

- [1] Siegel RL, Miller KD, Fuchs HE, et al. Cancer statistics, 2021 [J]. CA Cancer J Clin, 2021, 71(1):7-33.
- [2] Linehan WM, Ricketts CJ. The Cancer Genome Atlas of renal cell carcinoma: findings and clinical implications [J]. Nat Rev Urol, 2019, 16(9):539-552.
- [3] Hayes AR, Grossman AB. The ectopic adrenocorticotrophic hormone syndrome: rarely easy, always challenging [J]. Endocrinol Metab Clin North Am, 2018, 47(2):409-425.
- [4] Ru F, Chen X, Zhang B. Application of 3D printing technology in endophytic reninoma: a case report and literature review [J]. Clin Nephrol, 2021, 96(3):179-183.
- [5] Feng CC, Ding GX, Song NH, et al. Paraneoplastic hormones: parathyroid hormone-related protein (PTHrP) and erythropoietin (EPO) are related to vascular endothelial growth factor (VEGF) expression in clear cell renal cell carcinoma [J]. Tumour Biol, 2013, 34(6):3471-3476.
- [6] Ikuerowo SO, Ojewuyi OO, Omisano OA, et al. Paraneoplastic syndromes and oncological outcomes in renal cancer [J]. Niger J Clin Pract, 2019, 22(9):1271-1275.
- [7] 杨瑜, 毛全宗, 李汉忠, 等. 泌尿系统恶性肿瘤副肿瘤综合征的临床特点及意义 [J]. 中华医学杂志, 2010, 90(48):3411-3414.
Yang Y, Mao QZ, Li HZ, et al. Clinical features of urological malignancies with paraneoplastic syndromes [J]. Natl Med J China, 2010, 90(48):3411-3414.
- [8] 谢焱, 李汉忠, 张寅生, 等. 肾癌所致骨软化症一例报告及文献复习 [J]. 中华泌尿外科杂志, 2011, 32(1):27-30.
Xie Y, Li HZ, Zhang YS, et al. Oncogenic osteomalacia in renal cell carcinoma: a case report and literature review [J]. Chin J Urology, 2011, 32(1):27-30.
- [9] 罗梦, 熊六波, 范红. 以顽固性剧烈咳嗽为主要表现的肾癌一例及文献复习 [J]. 国际呼吸杂志, 2021, 41(9):665-670.
Luo M, Xiong LB, Fan H. Renal cell carcinoma presenting with intractable and severe cough: one case report and literature review [J]. Inter J Respiratory, 2021, 41(9):665-670.
- [10] 邹泓, 庞丽娟, 胡文浩, 等. 肾细胞瘤的临床病理与免疫表型研究 [J]. 中华病理学杂志, 2008, 37(11):726-731.
Zou H, Pang LJ, Hu WH, et al. Study on clinicopathologic features and immunophenotype of 114 cases of renal cell carcinoma [J]. Chin J Pathol, 2008, 37(11):726-731.
- [11] Tacha D, Zhou D, Cheng L. Expression of PAX8 in normal and neoplastic tissues: a comprehensive immunohistochemical study [J]. Appl Immunohistochem Mol Morphol, 2011, 19(4):293-299.
- [12] 洪鹏, 刘茁, 刘承, 等. 转移性肾癌的治疗 [J]. 中华泌尿外科杂志, 2020, 41(6):474-476.
Hong P, Liu Z, Liu C, et al. The treatment for metastatic renal cell carcinoma [J]. Chin J Urology, 2020, 41(6):474-476.
- [13] Bindayi A, Hamilton ZA, McDonald ML, et al. Neoadjuvant therapy for localized and locally advanced renal cell carcinoma [J]. Urol Oncol, 2018, 36(1):31-37.
- [14] Hegemann M, Kroeger N, Stenzl A, et al. Rare and changeable as a chameleon: paraneoplastic syndromes in renal cell carcinoma [J]. World J Urol, 2018, 36(6):849-854.
- [15] 叶雄俊, 阮永同, 熊六林, 等. 多发转移性肾癌舒尼替尼新辅助治疗后减瘤手术一例报告并文献复习 [J]. 中华泌尿外科杂志, 2013, 34(6):466-469.
Ye XJ, Ruan YT, Xiong LL, et al. Multiple metastatic renal cell carcinoma treated with cytoreductive nephrectomy after neoadjuvant Sunitinib therapy: a case report and literature review [J]. Chin J Urology, 2013, 34(6):466-469.
- [16] Powles T, Albiges L, Staehler M, et al. Updated European association of urology guidelines: recommendations for the treatment of first-line metastatic clear cell renal cancer [J]. Eur Urol, 2018, 73(3):311-315.
- [17] 邓建华, 纪志刚. 高危肾细胞癌术前新辅助靶向药物治疗 [J]. 现代泌尿外科杂志, 2018, 23(6):405-408.
Deng JH, Ji ZG. Neoadjuvant targeted drug therapy for high risk renal cell carcinoma [J]. J Mod Urol, 2018, 23(6):405-408.
- [18] 何先东, 韩博, 吴舜, 等. 原发灶减瘤术对肾癌肺转移患者预后的影响 [J]. 西南国防医药, 2020, 30(2):96-99.
He XD, Han B, Wu S, et al. Effects of CN on prognosis for RCC patients with pulmonary metastasis [J]. Med J Natl Defending Forces Southwest China, 2020, 30(2):96-99.
- [19] Hanna N, Sun M, Meyer CP, et al. Survival analyses of patients with metastatic renal cancer treated with targeted therapy with or without cytoreductive nephrectomy: a national cancer data base study [J]. J Clin Oncol, 2016, 34(27):3267-3275.

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- [9] 刘耀先, 连方. 连方中药调周疗法治疗经后三期经验 [J]. 江西中医药, 2015, 46(10):26-28.
Liu YX, Lian F. Lian Fang's experience in the treatment of postmenstrual three stages with traditional Chinese Medicine [J]. Jiangxi J Tradit Chin Med, 2015, 46(10):26-28.
- [10] 李杰, 张建伟, 陈艳花. 连方治疗先兆流产的经验 [J]. 江苏中医药, 2012, 44(3):9-10.
Li J, Zhang JW, Chen YH. Experience of Lian Fang in treating threatened abortion [J]. Jiangsu J Tradit Chin Med, 2012, 44(3):9-10.
- [11] 常敏毅. 日华子本草辑注 [M]. 北京: 中国医药科技出版社, 2016:71.
Chang MY. Annotation to the Rihuazi Materia Medica [M]. Beijing: China Medical Science and Technology Press, 2016:71.

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