doi: 10.13241/j.cnki.pmb.2017.15.030

氟康唑胶囊联合知柏地黄丸治疗滴虫性阴道炎的疗效及对患者血清IL-10和TNF-α水平的影响*

王少丽[1] 韩 蓁[2] 董 晋[1] 张 明[1] 谭秋花[1]

（1陕西省妇幼保健院 妇科 陕西 西安 710061；2西安交通大学第一附属医院 妇科 陕西 西安 710061）

摘要 目的：探讨氟康唑胶囊联合知柏地黄丸对滴虫性阴道炎患者血清白细胞介素-10(IL-10)、肿瘤坏死因子-α(TNF-α)的影响及临床疗效。**方法：**收集我院就诊的78例滴虫性阴道炎患者，随机分为实验组和对照组，各39例。对照组患者给予氟康唑胶囊治疗，实验组在对照组基础上给予知柏地黄丸治疗。观察并比较两组患者治疗前后IL-10、TNF-α、阴道健康评分及临床疗效。**结果：**与治疗前相比，两组患者治疗后血清IL-10、TNF-α水平均显著下降，阴道健康评分均明显升高，差异具均有统计学意义(P<0.05)；与对照组相比，实验组患者治疗后血清IL-10、TNF-α水平较低，阴道健康评分和临床治疗总有效率均较高，差异均具有统计学意义(P<0.05)。**结论：**氟康唑胶囊联合知柏地黄丸能够有效提高滴虫性阴道炎患者的临床疗效，可能与其显著降低血清IL-10、TNF-α水平有关。

关键词：氟康唑胶囊；知柏地黄丸；滴虫性阴道炎；白细胞介素-10；肿瘤坏死因子-α

中图分类号：R711.31 **文献标识码：**A **文章编号：**1673-6273(2017)15-2917-03

Effect of Fluconazole Capsules Combined with Zhibaidihuangwan on the Serum Levels of IL-10 and TNF-α and Clinical Effect of Patients with Trichomonas Vaginitis*

WANG Shao-li[1], HAN Zhen[2], DONG Jin[1], ZHANG Ming[1], TAN Qiu-hua[1]

(1 Department of Gynecology, maternal and child health care hospital of Shaanxi, Xi'an, Shaanxi, 710061, China;

2 Department of Gynecology, the First Affiliated Hospital, Xi'an Jiao Tong University, Xi'an, Shaanxi, 710061, China)

ABSTRACT Objective: To investigate the effect of fluconazole capsule combined with Zhibaidihuangwan on the serum IL-10, TNF-α levels and clinical effect of patients with trichomonas vaginitis. **Methods:** 78 cases of trichomonas vaginitis patients were collected in our hospital and randomly divided into the experimental group and control group, with 39 cases in each group. Patients in the control group were treated with fluconazole, and patients in the experimental group were treated with fluconazole AND Zhibaidihuangwan. Then the changes of serum levels of interleukin-10 (IL-10) and tumor necrosis factor alpha (TNF-α) and the vaginal health score as well as the clinical efficacy were observed and compared before and after treatment. **Results:** Compared with before treatment, the serum TNF-α, IL-10 levels in both groups of patients after treatment were decreased, the vagina health score were significantly increased(P<0.05); compared with the control group, the serum IL-10, TNF-α levels were obviously lower of patients in the experimental group, the vagina health score and total efficiency were significantly higher of patients in the experimental group(P<0.05). **Conclusion:** Fluconazole capsule combined with Zhibaidihuangwan could effectively enhance the clinical curative effect of trichomonad vaginitis patients, which might be related to the reduction of serum IL-10 and TNF-α levels.

Key words: Fluconazole Capsules; Zhibaidihuang pill; Trichomonas vaginitis; IL-10; TNF-α

Chinese Library Classification(CLC): R711.31 Document code: A

Article ID: 1673-6273(2017)15-2917-03

前言

滴虫性阴道炎(trichomonasvaginalis，TV)是一种由阴道毛滴虫引起的临床常见的妇科炎症之一[1]。阴道毛滴虫呈梨形，多透明无色，生命力强，能存活较长时间[2]。患者以稀薄灰白的泡沫状有臭味的白带为主要的临床症状，伴有外阴的瘙痒、烧灼感，还可有性交痛，部分患者还可伴有尿频、尿痛等症状[3]。有研究表明约60%的滴虫性阴道炎患者合并有细菌性阴道疾病[4]。阴道毛滴虫还能影响精子在阴道内生存。临床治疗滴虫性阴道炎首选药物为硝基咪唑类药物，且多为局部给药，但目前发现药物的耐药性不断升高，滴虫无法彻底被消灭，导致患者的疗效不断降低[5]。氟康唑是三唑类抗真菌药的一种，对多种真菌具有广谱抗菌作用，能够特异性地使真菌细胞失去酶活性，从而影响真菌的合成，还能够使菌内过氧化物积聚，最终造成菌体

* 基金项目：陕西省自然科学基金项目(2010H091)

作者简介：王少丽(1974-)，女，硕士，主治医师，研究方向：妊娠期高血压、产后出血等，电话：13186147151

(收稿日期：2016-10-28 接受日期：2016-11-21)

的死亡[6]。氟康唑主要经肾脏排泄,无明显的肝脏毒性,经口服吸收率高,因此临床疗效较好。祖国医学中没有"滴虫性阴道炎"的具体病名,但根据其临床表现,可将其归于"带下病"及"阴痒"等范畴,多是由冲任不固、湿热之邪入侵所致[7]。本实验选用氟康唑胶囊联合知柏地黄丸治疗滴虫性阴道炎,通过观察治疗前后患者血清 IL-10、TNF-α 水平,探讨氟康唑胶囊联合知柏地黄丸的治疗滴虫性阴道炎的临床效果及可能机制,现报道如下。

1 资料与方法

1.1 临床资料

收集 2015 年 3 月 ~2016 年 6 月于我院就诊的 78 例滴虫性阴道炎患者,随机分为实验组和对照组两组,组内各 39 例。两组患者均为女性,对照组以及对照组患者平均年龄分别为(32.86± 0.95)岁和(33.17± 0.91)岁;所有患者均符合《滴虫性阴道炎诊治规范》中关于滴虫性阴道炎的诊断标准,并经阴道分泌物检测确诊。所有患者无引导混合感染,实验前未口服或引导冲洗使用过抗生素或激素,无感染性疾病,无内分泌疾病以及免疫系统疾病,实验前均未使用过激素类药物或实验相关药物,对实验药物无过敏反应,均签署知情同意书同意进行实验。两组患者一般资料比较均无明显差异(P>0.05),具有可比性。

1.2 治疗方法

两组患者入院后均给予相应的治疗措施,对照组患者给予氟康唑胶囊 (国药准字 H20034164 广州柏赛罗药业有限公司) 0.2 g/ 次,1 次 /d;实验组患者在对照组的基础上给予知柏地黄丸(国药准字 Z42020477,湖北御金丹药业有限公司)8 丸 / 次,3 次 /d。治疗连续 4 周,治疗期间根据患者的情况,及时调整药量。

1.3 检测方法

1.3.1 **白细胞介素 -10(IL-10)水平检测** 治疗前后取外周静脉血 3 mL,离心取上清,采用 ELISA 法对患者血清白细胞介素－10(IL-10)水平进行检测。

1.3.2 **肿瘤坏死因子 -α(TNF-α)水平检测** 治疗前后取外周静脉血 3mL,离心取上清,采用酶联免疫吸附法,对患者血清 TNF-α 水平进行检测。

1.4 阴道健康评分

治疗前后对患者的阴道健康情况进行检测,对患者的阴道褶皱、pH 值、湿润度、粘膜情况以及分泌物情况进行检测,正常为 4 分,最低为 1 分,pH 值低于 4.5 为 4 分,4.5~5 为 3 分,5.1~6 为 2 分,pH 值在 6 以上为 1 分,计算患者的总分为阴道健康状况评分。

1.5 疗效评价

患者治疗后对患者的临床疗效进行评价:患者治疗后泡沫状或脓性白带消失,阴道充血症状明显减轻,阴道分泌物悬滴液镜检滴虫呈阴性为痊愈;患者治疗后临床症状以及体征缓解,阴道分泌物悬滴液镜检滴虫呈阳性为有效;患者治疗后临床症状无明显改善甚至加重,阴道分泌物悬滴液镜检滴虫呈阳性为无效。

1.6 统计学分析

采用 SPSS19.0 统计软件进行分析,计量数据以均数± 标准差($\bar{x}$± s)表示,采用 t 检验;计数资料用%表示,采用卡方检验。以 P<0.05 认为差异有统计学意义。

2 结果

2.1 两组患者临床疗效比较

治疗后,实验组患者治疗总有效率显著高于对照组(P<0.05),见表 1。

表 1 两组患者临床疗效比较【例(%)】

Table 1 Comparison of the clinical curative effect between two groups[n(%)]

Groups	Cure	Effective	Invalid	Total effective rate
Experimental group	27(69.23)	10(25.64)	2(5.13)	37(94.87)*
Control group	15(38.46)	14(35.90)	10(25.64)	29(74.36)

Note: Compared with the control group, *P<0.05.

2.2 两组患者治疗前后阴道健康评分比较

治疗后,两组患者的阴道健康评分水平与治疗前相比均显著升高 (P<0.05),实验组患者的阴道健康评分与对照组较高(P<0.05),见表 2。

表 2 两组患者治疗前后阴道健康评分比较($\bar{x}$± s)

Table 2 Comparison of the vaginal health score between two groups before and after treatment($\bar{x}$± s)

Groups	Before treatment	After treatment
Experimental group	6.01± 1.01	12.24± 0.71*#
Control group	6.67± 0.89	10.02± 0.52*

Note: Compared with before treatment, *P<0.05; Compared with the control group after treatment, #P<0.05.

2.3 两组患者治疗前后血清 IL-10 水平比较

治疗后,两组患者血清 IL-10 水平与治疗前相比下降(P<0.05),实验组患者 IL-10 水平与对照组相比较低(P<0.05),见表3。

表 3 两组患者治疗前后 IL-10 水平比较 (pg/mL,$\bar{x}$± s)

Table 3 Comparison of the serum levels of IL-10 between two groups before and after treatment (pg/mL, $\bar{x}$± s)

Groups	Before treatment	After treatment
Experimental group	81.72± 16.04	21.35± 10.01*#
Control group	84.01± 13.36	31.06± 13.78*

Note: Compared with before treatment, *P<0.05; Compared with the control group after treatment, #P<0.05.

2.4 两组患者治疗前后 TNF-α 水平比较

治疗后,两组患者的血清 TNF-α 水平与治疗前相比下降(P<0.05),实验组患者的血清 TNF-α 水平与对照组相比较低(P<0.05),见表 4。

表 4 两组患者治疗前后 TNF-α 水平比较(pg/L，$\bar{x}\pm s$)

Table 4 Comparison of the serum levels of TNF-α between two groups before and after treatment (pg/L, $\bar{x}\pm s$)

Groups	Before treatment	After treatment
Experimental group	89.83± 12.73	17.33± 6.63*#
Control group	91.27± 10.78	38.12± 9.18*

Note: Compared with before treatment, *P<0.05; Compared with the control group after treatment, #P<0.05.

3 讨论

滴虫性阴道炎与不孕、早产等的发生有关，还可加速人类免疫缺陷病毒的传播。健康女性阴道微生态环境的平衡，由阴道内各种微生物之间的相互协调维持[8]。正常女性阴道含有乳酸杆菌，将阴道维持在酸性环境下，能够抑制阴道毛滴虫的生长，当生殖系统功能失调，阴道环境变为碱性，滴虫增殖，导致阴道炎的发生[9]。研究证实[10]阴道毛滴虫能够吞噬精子，诱发不孕的发生，而且提高了患者宫颈癌的发病率。滴虫性阴道炎在祖国医学中属＂带下病＂、＂阴痒＂等的范畴，多是由于冲任不固、湿热入侵而致。知柏地黄丸首载于《医宗金鉴》，具有滋肾益阴，清虚火的功效。方中熟地黄滋阴养血，知母能够清热滋阴，可治阴虚火旺所致的各种疾病[11]。黄柏清热燥湿，山药益气养阴，具有补脾肾的功效，山萸萸补益肝肾，茯苓利水渗湿，经现代研究表明[12]，知母可以升高血皋皮质醇浓度，预防肾上腺的萎缩，山药能够增强免疫力、抗衰老，茯苓具有抑制细菌的生长的作用。诸药合用，对滴虫性阴道炎具有较好的疗效。本研究结果显示氟康唑胶囊联合知柏地黄丸治疗的滴虫性阴道炎患者疗效较单用氟康唑胶囊更好。

Th 细胞具有抵御外来病原体的作用，当 Th1 细胞相对含量较高时，病情趋向痊愈，Th2 相对含量较高时，患者的病情趋向严重[13]。白介素 -10(IL-10)属于 Th2 型细胞因子，主要由 Th2 细胞、单核细胞等产生，具有多功能的负性调节，主要参与体内的体液免疫反应过程，IL-10 是重要的炎症抑制性细胞因子，可明显抑制 TNF-α 等炎性介质的表达[14-16]。当炎症反应发生时，血清 IL-10 水平将会发生明显的升高。因此，IL-10 也能够反应机体免疫水平，IL-10 还具有抑制单核细胞分化的作用，也能够抑制 NK 细胞的杀伤能力[17]。外来微生物的侵袭会造成 IL-10 水平的升高。本实验结果显示：两组患者治疗后的 IL-10 水平均下降，氟康唑胶囊联合知柏地黄丸治疗的患者的 IL-10 水平较低。TNF-α 由巨噬细胞以及单核细胞产生，能够刺激单核巨噬细胞等细胞产生细胞因子，参与炎性反应过程，在病理状态下，TNF-α 的水平显著升高[18]。有研究证实在机体发生炎症反应时，TNF-α 的水平升高[19,20]。本实验结果显示两组患者治疗后的血清 TNF-α 水平下降，康唑胶囊联合知柏地黄丸治疗患者的血清 TNF-α 水平较低，提示康唑胶囊联合知柏地黄丸治疗能够更有效抑制体内的炎症反应，进而对滴虫性阴道炎产生较好的治疗作用。

总之，本研究结果表明氟康唑胶囊联合知柏地黄丸能够有效提高滴虫性阴道炎患者的临床疗效，可能与其显著降低血清 IL-10、TNF-α 水平有关。

参 考 文 献(References)

[1] Lazenby G B, Taylor P T, Badman B S, et al. An association between Trichomonas vaginalis and high-risk human papillomavirus in rural Tanzanian women undergoing cervical cancer screening [J]. Clinical therapeutics, 2014, 36(1): 38-45

[2] Silver B J, Guy R J, Kaldor J M, et al. Trichomonas vaginalis as a cause of perinatal morbidity: a systematic review and meta-analysis [J]. Sexually transmitted diseases, 2014, 41(6): 369-376

[3] Twu O, Dessí D, Vu A, et al. Trichomonas vaginalis homolog of macrophage migration inhibitory factor induces prostate cell growth, invasiveness, and inflammatory responses [J]. Proceedings of the National Academy of Sciences, 2014, 111(22): 8179-8184

[4] Huang K Y, Chen Y Y M, Fang Y K, et al. Adaptive responses to glucose restriction enhance cell survival, antioxidant capability, and autophagy of the protozoan parasite Trichomonas vaginalis[J]. Biochimica et Biophysica Acta (BBA)-General Subjects, 2014, 1840(1): 53-64

[5] Masson L, Mlisana K, Little F, et al. Defining genital tract cytokine signatures of sexually transmitted infections and bacterial vaginosis in women at high risk of HIV infection: a cross-sectional study[J]. Sexually transmitted infections, 2014, 90(8): 580-587

[6] Secor W E, Meites E, Starr M C, et al. Neglected parasitic infections in the United States: trichomoniasis[J]. The American journal of tropical medicine and hygiene, 2014, 90(5): 800-804

[7] Olowe O, Makanjuola O, Olowe R, et al. Prevalence of vulvovaginal candidiasis, trichomoniasis and bacterial vaginosis among pregnant women receiving antenatal care in Southwestern Nigeria[J]. European Journal of Microbiology and Immunology, 2014, 4(4): 193-197

[8] Lazenby G B, Unal E R, Andrews A L, et al. Cost-effectiveness analysis of annual Trichomonas vaginalis screening and treatment in HIV-positive women to prevent HIV transmission [J]. Sexually transmitted diseases, 2014, 41(6): 353-358

[9] Seo M Y, Im S J, Gu N Y, et al. Inflammatory response of prostate epithelial cells to stimulation by Trichomonas vaginalis[J]. The Prostate, 2014, 74(4): 441-449

[10] Der Pol B, Williams J A, Taylor S N, et al. Detection of Trichomonas vaginalis DNA by use of self-obtained vaginal swabs with the BD ProbeTec Qx assay on the BD Viper system[J]. Journal of clinical microbiology, 2014, 52(3): 885-889

[11] Fastring D R, Amedee A, Gatski M, et al. Co-occurrence of Trichomonas vaginalis and bacterial vaginosis and vaginal shedding of HIV-1 RNA[J]. Sexually transmitted diseases, 2014, 41(3): 173-179

[12] Hirt R P, Sherrard J. Trichomonas vaginalis origins, molecular pathobiology and clinical considerations [J]. Current opinion in infectious diseases, 2015, 28(1): 72-79

[13] Hezarjaribi H Z, Fakhar M, Shokri A, et al. Trichomonas vaginalis infection among Iranian general population of women: a systematic review and meta-analysis [J]. Parasitology research, 2015, 114 (4): 1291-1300

[14] Smith J, Garber G E. Current status and prospects for development of a vaccine against Trichomonas vaginalis infections[J]. Vaccine, 2014, 32(14): 1588-1594

（下转第 2891 页）

ysis patients[J]. Saudi Pharm J, 2015, 23(5): 544-548

[3] KDIGO Anemia Work Group. KDIGO clinical practice guideline for anemia in chronic kidney disease [J]. Kidney inter, 2012, 2(Suppl): 297-335

[4] Ghanta M, Jim B. Renal Transplantation in advanced chronic kidney disease patients[J]. Med Clin North Am, 2016,100(3): 465-476

[5] Qamar A, Bhatt DL. Stroke prevention in atrial fibrillation in patients with chronic kidney disease [J]. Circulation, 2016, 133 (15): 1512-1515

[6] Roxo RS, Xavier VB, Miorin LA, et al. Impact of neuromuscular electrical stimulation on functional capacity of patients with chronic kidney disease on hemodialysis[J]. J Bras Nefrol, 2016, 38(3): 344-350

[7] Elsheikh N, Sherif N, Zeid SA, et al. The link between bone disease and cardiovascular complication in hemodialysis patients[J]. Electron Physician, 2016, 8(6): 2483-2488

[8] Kawahito K, Aizawa K, Oki S, et al. Heart valve surgery in hemodialysis-dependent patients: nutrition status impact on surgical outcome[J]. J Artif Organs, 2016, 19(2): 134-140

[9] Michels WM, Jaar BG, Ephraim PL, et al. Intravenous iron administration strategies and anemia management in hemodialysis patients[J]. Nephrol Dial Transplant, 2016, 6 [Epub ahead of print]

[10] Fishbane S. Balance of benefit and risk in intravenous iron treatment in chronic kidney disease[J]. Semin Nephrol, 2016, 36(2): 124-129

[11] Liang R, Ghaffari S. Advances in understanding the mechanisms of erythropoiesis in homeostasis and diseases [J]. Br J Haematol, 2016, 174(5): 661-673

[12] Zhang H, Li X, Kan Y, et al. Analysis of the correlation between serum resistin and the variability of erythropoietin responsiveness in patients with chronic kidney disease [J]. Exp Ther Med, 2015, 10(5): 1925-1930

[13] Hertzberg-Bigelman E, Barashi R, Levy R, et al. Down-regulation of cardiac erythropoietin receptor and its downstream activated signal transducer phosphor-STAT-5 in a rad model of chronic kidney disease[J]. Isr Med Assoc J, 2016, 18(6): 326-330

[14] Sanchez-Gonzalez LR, Castro-Melendez SE, Angeles-Torres AC, et al. Efficacy and safety of adjuvant recombinant human erythropoietin and ferrous sulfate as treatment for iron deficiency anemia during the third trimester of pregnancy [J]. Eur J Obstet Gynecol Reprod Biol, 2016, 205: 32-36

[15] Briet M, Barhoumi T, Mian MO, et al. Effects of recombinant human erythropoietin on resistance artery endothelial function in stage 4 chronic kidney disease[J]. J Am Heart Assoc, 2013, 2(2): e000128

[16] Teixeira M, Rodrigues-Santos P, Garrido P, et al. Cardiac antiapoptotic and proproliferative effect of recombinant huan erythropoietin in a moderate stage of chronic renal failure in the rat [J]. J Pharm Bioallied Sci, 2012, 4(1): 76-83

[17] Honda H, Kimata N, Wakai K, et al. Associations among epoetin therapy, inflammation, nutritional status, and mortality in patients on hemodialysis[J]. J Ren Nutr, 2014, 24(5): 322-329

[18] Jasiulewicz A, Lisowska KA, Debska-Slizien A, et al. Phenotype, proliferation and apoptosis of B lymphocytes in hemodialysis patients treated with recombinant human erythropoietin [J]. Int Immunol, 2016,8 [Epub ahead of print]

[19] Ribeiro S, Garrido P, Fernandes J, et al. Renal risk-benefit determinants of recombinant human erythropoietin therapy in the remnant kidney rat model - hypertension, anaemia, inflammation and drug dose[J]. Clin Exp Pharmacol Physiol, 2016, 43(3): 3443-3454

[20] Hu JP, Cheng X, Xu XF, et al. Reactivity of patients with maintenance hemodialysis to erythropoietin in the treatment of renal anemia [J]. J Biol Regul Homeost Agents, 2016, 30(2): 535-540

（上接第 2919 页）

[15] Henning T R, Butler K, Hanson D, et al. Increased susceptibility to vaginal simian/human immunodeficiency virus transmission in pig-tailed macaques coinfected with Chlamydia trachomatis and Trichomonas vaginalis [J]. Journal of Infectious Diseases, 2014, 210(8): 1239-1247

[16] Seña A C, Bachmann L H, Hobbs M M. Persistent and recurrent Trichomonas vaginalis infections: epidemiology, treatment and management considerations[J]. Expert review of anti-infective therapy, 2014, 12(6): 673-685

[17] Valadkhani Z. Role of pH on Adhesion of Trichomonas Vaginalis Isolated from Symptomatic & Asymptomatic Women to Vaginal Epithelial Cells in Vitro [J]. Iranian Journal of Medical Sciences, 2015, 29(3): 134-139

[18] Han C, Wu W, Fan A, et al. Diagnostic and therapeutic advancements for aerobic vaginitis [J]. Archives of gynecology and obstetrics, 2015, 291(2): 251-257

[19] Miranda A E, Pinto V M, Gaydos C A. Trichomonas vaginalis infection among young pregnant women in Brazil [J]. Brazilian Journal of Infectious Diseases, 2014, 18(6): 669-671

[20] Arbabi M, Fakhrieh Z, Delavari M, et al. Prevalence of Trichomonas vaginalis infection in Kashan city, Iran (2012-2013)[J].International Journal of Reproductive BioMedicine, 2014, 12(7): 507-512