

doi: 10.13241/j.cnki.pmb.2020.12.024

玉屏风散联合头孢丙烯对鼻炎患者免疫功能及应激损伤程度的影响 *

唐幸一 李一奇 孙宣东 李伟忠 肖 栋[△]

(无锡市江南大学附属医院(无锡三院)耳鼻咽喉科 江苏 无锡 214000)

摘要 目的:探讨玉屏风散联合头孢丙烯对鼻炎患者免疫系统及应激损伤程度的影响。**方法:**将2016年8月~2018年2月我院收治的鼻炎患者120例按照随机数字表法分为对照组与观察组,每组60例。对照组患者给予头孢丙烯治疗;观察组患者给予玉屏风散联合头孢丙烯治疗。两组患者均连续治疗14天。分别于治疗前后检测并比较两组患者血清环磷酸腺苷(cAMP)、环磷酸鸟苷(cGMP)、免疫球蛋白E(Ig E)、辅助T细胞1/辅助T细胞2(Th1/Th2)、一氧化氮(NO)、丙二醛(MDA)、超氧化物歧化酶(SOD)、C反应蛋白(CRP)、肿瘤坏死因子-α(TNF-α)及γ-干扰素(IFN-γ)水平的变化。**结果:**治疗后:两组患者血清cAMP、Th1/Th2比值及SOD水平较治疗前显著升高;cGMP、IgE、NO、MDA、CRP、TNF-α及IFN-γ水平较治疗前显著降低($P<0.05$),且观察组患者血清cAMP、Th1/Th2比值及SOD水平明显高于对照组,cGMP、IgE、NO、MDA、CRP、TNF-α及IFN-γ水平明显低于对照组($P<0.05$)。**结论:**玉屏风散联合头孢丙烯治疗鼻炎患者可提高患者免疫功能,同时减轻氧化应激及炎症反应损伤。

关键词:玉屏风散;鼻炎;免疫功能;氧化应激;炎症损伤**中图分类号:**R765.21;R242 **文献标识码:**A **文章编号:**1673-6273(2020)12-2313-04

Effect of Yupingfeng San Combined with Cefalexin on the Immune Function and Stress Injury in Patients with Rhinitis*

TANG Xing-yi, LI Yi-qi, SUN Xuan-dong, LI Wei-zhong, XIAO Dong[△]

(Department of Otolaryngology, Affiliated Hospital of Jiangnan University (Wuxi Third Hospital), Wuxi, Jiangsu, 214000, China)

ABSTRACT Objective: To investigate the effect of Yupingfeng San combined with Cefalexin on immune system and stress injury in patients with rhinitis. **Methods:** 120 patients with rhinitis admitted to our hospital from August 2016 to February 2018 were randomly divided into control group and observation group, 60 cases in each group. The patients in the control group were treated with cefalexin, while those in the observation group were treated with Yupingfeng San and cefalexin. Patients in both groups were treated continuously for 14 days. The serum levels of Cyclic adenosine monophosphate (cAMP), cyclic guanosine monophosphate (cGMP), immunoglobulin E (Ig E), helper T cell 1/helper T cell 2(Th1/Th2), nitric oxide (NO), malondialdehyde (MDA), superoxide dismutase (SOD), C-reactive protein (CRP), tumor necrosis factor-α (TNF-α) and interferon-γ (IFN-γ) in serum of the patients in the two groups were detected and compared before and after treatment. **Results:** After treatment, the serum levels of cAMP, Th1/Th2 ratio and SOD of patients in the control group were significantly higher than those before treatment, while the levels of cGMP, IgE, NO, MDA, CRP, TNF-α and IFN-γ were significantly lower than those before treatment ($P<0.05$). After treatment, the changes of serum levels of these factors in the observation group were the same as those in the control group. The serum levels of cAMP, Th1/Th2 ratio and SOD of patients in the observation group were significantly higher than those in the control group, and the levels of cGMP, IgE, NO, MDA, CRP, TNF-α and IFN-γ of patients in the observation group were significantly lower than those in the control group ($P<0.05$). **Conclusion:** Yupingfeng San combined with Cefalexin has significant clinical effect in the treatment of rhinitis. Yupingfeng San can improve the immune function of patients by regulating the levels of cytokines, and at the same time reduce oxidative stress and inflammatory reaction damage.

Key words: Yupingfeng San; Rhinitis; Immune Function; Oxidative Stress; Inflammatory Injury**Chinese Library Classification(CLC):** R765.21; R242 **Document code:** A**Article ID:** 1673-6273(2020)12-2313-04

前言

变应性鼻炎及过敏性鼻炎是由变应原引起的鼻腔黏膜非感染性的炎症疾病^[1-3],其临床表现主要为鼻腔黏膜充血、

肿胀、渗出、增生、萎缩或坏死等,严重影响患者生活质量^[4-6]。西医指出鼻炎主要发病因素为口鼻道复合体发生阻塞,通气引流功能出现异常,鼻腔中细菌快速繁殖,导致出现粘膜炎症。头孢丙烯^[7]为头孢菌素类第二代光谱杀菌素,结构为顺反式异构体

* 基金项目:江苏省人力和社会保障厅“六大人才高峰”计划项目(2014-WSW-060)

作者简介:唐幸一(1984-),女,住院医师,主要从事耳鼻咽喉科方面的疾病诊治工作,电话:13405781158,E-mail:txy8763@163.com

△ 通讯作者:肖栋,硕士研究生,主治医师,主要从事耳鼻咽喉科方面的疾病诊治工作

(收稿日期:2019-10-23 接受日期:2019-11-19)

混合物,其中顺式异构体占比为90%以上,在MIC期就表现出一定的杀菌效果,对流感嗜血杆菌、金葡菌、化脓链球菌等表现出一定的杀伤力;然而,单独头孢丙烯西药治疗,患者易出现耐药性,并未获得较佳的临床效果。

研究表明中西结合治疗会表现出较好的疗效^[7,8];玉屏风散是临床常用中药制剂,由防风、黄芪、白术(炒)三味中药组成,三者共同共奏补中有散,共建益气,固表止汗之功。研究表明玉屏风散具有调节机体免疫功能、提高机体抗氧化能力的作用^[7,9]。本次研究初步探讨了玉屏风散与头孢丙烯联合应用治疗变应性鼻炎对患者免疫系统及氧化/炎性应激损伤程度的影响。

1 资料与方法

1.1 一般资料

收集2016年8月~2018年2月无锡市江南大学附属医院收治的变应性鼻炎患者120例,采用随机数字表法分将其为对照组与观察组,每组各60例。入选患者均签署临床研究知情同意书。对照组患者60例,男33例,女27例;年龄35~62岁;病程3~8年。观察组患者60例,男29例,女31例;年龄32~65岁;病程2~10年。入选标准:^①符合《变应性鼻炎的诊治原则和推荐方案的标准》^[10]中关于变应性鼻炎的诊断标准;^②年龄18~65岁;^③病程≥1年;^④入院前1个月内未接受相关治疗。排除标准:^⑤合并鼻中隔偏曲;^⑥对本次研究所用玉屏风散及头孢丙烯过敏;^⑦合并皮肤过敏;^⑧合并严重心、肝、肾疾病者;^⑨妊娠期及哺乳期妇女。本院伦理委员会已批准此研究,两组一般临床资料比较无统计学差异,具有可比性。

1.2 治疗方法

对照组患者给予头孢丙烯片(南京亿华药业有限公司,国药准字:H20041960)治疗:口服,1片/次,2次/d。观察组患者在对照组治疗基础上,给予玉屏风散(建嘉制药有限公司,批号:HKP-06701)治疗:水煎服,10g/次,2次/d。两组患者均连续治疗14d。

1.3 观察指标

治疗前后,采集两组患者静脉血5mL,离心操作后取上层血清。利用酶联免疫吸附(ELISA)法检测血清中环磷酸腺苷(cAMP)、环磷酸鸟苷(cGMP)、免疫球蛋白E(Ig E)、超氧化物歧化酶(SOD)、C反应蛋白(CRP)、肿瘤坏死因子-α(TNF-α)及γ-干扰素(IFN-γ)水平,采用流式技术检测并计算Th1/Th2比值;利用硝酸还原酶法检测一氧化氮(NO)水平;利用硫代巴比妥酸比色法检测丙二醛(MDA)水平。

1.4 统计学处理

数据采用SPSS22.0软件进行统计学分析。计量资料以($\bar{x} \pm s$)表示,组间比较采用t检验,以P<0.05为有统计学差异。

2 结果

2.1 两组治疗前后cAMP及cGMP水平的比较

治疗前,两组变应性鼻炎患者cAMP及cGMP水平无明显统计学差异(P>0.05)。治疗后:对照组患者血清cAMP及cGMP水平分别为:(1.29±0.15)ng/L、(2.42±0.25)ng/L,与治疗前比较差异显著(P<0.05);观察组患者血清cAMP及cGMP水平分别为:(1.65±0.17)ng/L、(2.11±0.20)ng/L,cAMP水平明显高于对照组,cGMP水平明显低于对照组(P<0.05)。见表1。

表1 两组治疗前后cAMP及cGMP水平比较($\bar{x} \pm s$)

Table 1 Comparison of the levels of cAMP and cGMP before and after treatment between two groups($\bar{x} \pm s$)

Groups	Number of cases	time	cAMP(ng/L)	cGMP(ng/L)
Control group	60	Before treatment	1.04±0.12	2.93±0.30
		After treatment	1.29±0.15*	2.42±0.25*
	t/P		10.081/0.000	10.116/0.000
Observation group	60	Before treatment	1.18±0.13	2.87±0.29
		After treatment	1.65±0.17**	2.11±0.20**
	t/P		17.011/0.000	16.711/0.000
	t _对 /P _对		12.300/0.000	7.500/0.000

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

2.2 两组治疗前后免疫功能指标的变化比较

治疗后,对照组患者血清中IgE及Th1/Th2比值水平分别为(79.43±8.01)kIU/L、(0.87±0.09),观察组患者血清IgE及Th1/Th2比值水平分别为(63.12±6.43)kIU/L及(1.12±0.14),观察组患者血清IgE水平明显低于对照组,Th1/Th2比值水平明显高于对照组患者(P<0.05)。见表2。

2.3 两组治疗前后氧化应激水平的比较

治疗前,两组变应性鼻炎患者NO、MDA及SOD水平比较无明显统计学差异(P>0.05)。治疗后,对照组患者NO、MDA及SOD水平分别为(58.45±6.04)μmol/L、(7.28±0.73)μmol/L、

(75.45±7.46)U/mL,观察组患者NO、MDA及SOD水平分别为(42.84±4.39)μmol/L、(4.72±0.51)μmol/L、(93.84±9.46)U/mL,且SOD水平明显高于对照组患者,NO及MDA水平明显低于对照组患者(P<0.05)。见表3。

2.4 两组治疗前后血清炎症因子水平的比较

治疗前,两组患者血清CRP、TNF-α及IFN-γ水平比较无明显差异(P>0.05)。治疗后,对照组患者血清中CRP、TNF-α及IFN-γ水平分别为(70.16±7.08)mg/L、(32.43±3.30)pg/mL、(57.51±5.82)pg/mL,观察组患者血清中CRP、TNF-α及IFN-γ水平分别为:(53.04±5.32)mg/L、(21.17±2.36)pg/mL、

(39.56 ± 4.05) pg/mL, 与治疗前比较均显著降低, 观察组患者 CRP、TNF- α 及 IFN- γ 水平均明显低于对照组患者 ($P < 0.05$)。

表 2 两组治疗前后免疫功能指标的比较($\bar{x} \pm s$)Table 2 Comparison of the index of immune function before and after treatment between two groups($\bar{x} \pm s$)

Groups	Number of cases	time	IgE(kIU/L)	Th1/Th2
Control group	60	Before treatment	119.27 \pm 12.05	0.65 \pm 0.07
		After treatment	79.43 \pm 8.01*	0.87 \pm 0.09*
	t/P		21.328/0.000	14.946/0.000
Observation group	60	Before treatment	118.35 \pm 11.94	0.69 \pm 0.06
		After treatment	63.12 \pm 6.43**#	1.12 \pm 0.14**#
	t/P		31.546/0.000	21.868/0.000
$t^{\text{对}}/P^{\text{对}}$			12.300/0.000	11.635/0.000

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

表 3 两组治疗前后氧化应激水平的比较($\bar{x} \pm s$)Table 3 Comparison of the levels of oxidative stress before and after treatment between two groups($\bar{x} \pm s$)

Groups	Number of cases	time	NO($\mu\text{mol}/\text{L}$)	MDA($\mu\text{mol}/\text{L}$)	SOD(U/mL)
Control group	60	Before treatment	70.04 \pm 7.01	9.15 \pm 0.94	50.12 \pm 5.08
		After treatment	58.45 \pm 6.04*	7.28 \pm 0.73*	75.45 \pm 7.46*
	t/P		9.702/0.000	12.171/0.000	21.739/0.000
Observation group	60	Before treatment	69.85 \pm 6.93	9.36 \pm 0.97	49.86 \pm 5.02
		After treatment	42.84 \pm 4.39**#	4.72 \pm 0.51**#	93.84 \pm 9.46**#
	t/P		25.504/0.000	32.796/0.000	31.810/0.000
$t^{\text{对}}/P^{\text{对}}$			16.194/0.000	22.268/0.000	11.824/0.000

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

表 4 两组治疗前后血清炎症因子水平的比较($\bar{x} \pm s$)Table 4 Comparison of the levels of inflammatory factors before and after treatment between two groups($\bar{x} \pm s$)

Groups	Number of cases	time	CRP(mg/L)	TNF- α (pg/mL)	IFN- γ (pg/mL)
Control group	60	Before treatment	98.37 \pm 9.86	68.59 \pm 6.92	83.87 \pm 8.41
		After treatment	70.16 \pm 7.08*	32.43 \pm 3.30*	57.51 \pm 5.82*
	t/P		18.002/0.000	36.534/0.000	19.964/0.000
Observation group	60	Before treatment	97.63 \pm 9.84	69.02 \pm 6.89	84.36 \pm 8.52
		After treatment	53.04 \pm 5.32**#	21.17 \pm 2.36**#	39.56 \pm 4.05**#
	t/P		30.877/0.000	50.891/0.000	36.785/0.000
$t^{\text{对}}/P^{\text{对}}$			14.974/0.000	21.498/0.000	19.609/0.000

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

3 讨论

变应性鼻炎为临床常见疾病,发病人群较广,具有反复发作、久治不愈、难以根治等特点^[11-13],其发病与机体免疫系统功能失衡有密切联系^[14-16],目前主要治疗方法为脱敏治疗及药物治疗,但效果不甚理想^[17-19]。近年来,中医药疗法治疗变应性鼻炎取得了一定的成效,但其作用机制尚未明确^[20-22]。cAMP 与 cGMP 是机体细胞内部一对作用相反且相互制约的,具有传递信息功能的物质,其比值变化与免疫功能水平有关^[23,24]。IgE 是

机体变态反应的主要介质,由其介导的炎症反应加重是变应性鼻炎的主要发病机制^[25,26]。Th1 及 Th2 同属于辅助性 T 细胞(Th 细胞),Th1 细胞参与细胞免疫和迟发性超敏性炎症反应;Th2 可辅助 B 细胞分化为抗体分泌细胞,参与体液免疫应答。Th1/Th2 比例失衡是变应性鼻炎发作的关键基础^[27]。本研究结果显示治疗结束后观察组患者 cAMP、Th1/Th2 比值水平明显高于对照组,cGMP、IgE 水平明显低于对照组,提示玉屏风散治疗变应性鼻炎的作用机制可能与改善其免疫功能水平有关。

既往研究显示在变应性鼻炎疾病进程中,氧化应激与炎性

反应可协同作用,通过形成正反馈机制起到加速疾病进程的作用^[28]。NO 可与患者体内氧离子结合,生成过氧化物,加重对细胞的氧化损伤。MDA 为体内过氧化反应的终极产物。SOD 具有清除机体内部氧化自由基的作用,可间接反映患者体内氧自由基的水平。CRP、TNF- α 及 IFN- γ 为机体内炎症因子,可直接反映机体炎性反应程度,还可进一步加重 T 淋巴系统紊乱状态^[29]。玉屏风散为传统中药制剂,由黄芪、白术(炒)、防风组成。其中,黄芪多糖可通过双向调节机体的免疫功能,起到抑制病毒及细菌感染的作用;白术多糖可增强机体清除自由基的能力,具有显著的抗氧化作用;防风多糖可增强机体免疫力、抗炎抑菌^[30]。本次研究结果显示:两组患者治疗后血清 SOD 水平与治疗前比较均显著升高,NO、MDA、CRP、TNF- α 及 IFN- γ 水平均显著降低;且观察组患者上述应激反应相关因子水平的变化趋势明显高于对照组患者,提示玉屏风散联合头孢丙烯治疗变应性皮炎可能通过调节患者体内抗氧化酶水平,抑制炎症因子产生及释放,起到缓解氧化应激及炎症反应损伤的作用。

综上所述,玉屏风散联合头孢丙烯治疗鼻炎患者可提高患者免疫功能,同时减轻氧化应激及炎症反应损伤。

参 考 文 献(References)

- [1] Niksarlıoğlu EY, İşik R, Uysal MA, et al. Prevalence of atopy and allergic rhinitis in patients with adult non-cystic fibrosis bronchiectasis[J]. Turk J Med Sci, 2019, 49(2): 551-557
- [2] Mahnashi TA, Faqih MA, Moafa AN, et al. Severity and prevalence of allergic rhinitis among school children, Jazan Region Saudi Arabia[J]. J Family Med Prim Care, 2019, 8(2): 663-668
- [3] Ziyab AH. Prevalence of food allergy among schoolchildren in Kuwait and its association with the coexistence and severity of asthma, rhinitis, and eczema: A cross-sectional study[J]. World Allergy Organ J, 2019, 12(4): 100024
- [4] Yang R, Zou Y, Qiao YL, et al. Characteristic analysis of Aeroallergens of allergic rhinitis patients in Wuhan [J]. Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi, 2019, 33(3): 267-271
- [5] Byeon H. The association between allergic rhinitis and otitis media: A national representative sample of in South Korean children [J]. Sci Rep, 2019, 9(1): 1610
- [6] Wang L, Lv Q, Song X, et al. ADRB2 suppresses IL-13-induced allergic rhinitis inflammatory cytokine regulated by miR-15a-5p [J]. Hum Cell, 2019, 32(3): 306-315
- [7] 李爽. 分析通窍鼻炎颗粒联合头孢丙烯治疗急性鼻炎临床效果[J]. 世界最新医学信息文摘, 2018(21): 143, 154
- [8] 杜坐平, 钱红娇. 玉屏风散辅助氯雷他定对小儿过敏性鼻炎患者疗效、免疫功能及 CRP 水平影响研究 [J]. 辽宁中医药大学学报, 2017, 19(11): 130-132
- [9] Zhou CJ, Ma F, Liao WJ, et al. Restoration of immune suppressor function of regulatory B cells collected from patients with allergic rhinitis with Chinese medical formula Yupingfeng San [J]. Am J Transl Res, 2019, 11(3): 1635-1643
- [10] 顾之燕, 董震. 变应性鼻炎的诊治原则和推荐方案[J]. 中华耳鼻咽喉头颈外科杂志, 2005, 40(03): 8-9
- [11] Sánchez-Borges M, Capriles-Hulett A, Torres J, et al. Diagnosis of allergic sensitization in patients with allergic rhinitis and asthma in a tropical environment[J]. Rev Alerg Mex, 2019, 66(1): 44-54
- [12] Nguyen SA, Camilon MP, Schlosser RJ. Identification of microbial contaminants in sinus rinse squeeze bottles used by allergic rhinitis patients [J]. World J Otorhinolaryngol Head Neck Surg, 2019, 5(1): 26-29
- [13] Lin SW, Wang SK, Lu MC, et al. Acute rhinosinusitis among pediatric patients with allergic rhinitis: A nationwide, population-based cohort study[J]. PLoS One, 2019, 14(2): e0211547
- [14] Zielen S, Plückhahn K, Akboga Y, et al. Fast up-dosing with a birch allergoid is safe and well tolerated in allergic rhinitis patients with or without asthma[J]. Immunotherapy, 2019, 11(3): 177-187
- [15] Heffler E, Brussino L, Del Giacco S, et al. New drugs in early-stage clinical trials for allergic rhinitis [J]. Expert Opin Investig Drugs, 2019, 28(3): 267-273
- [16] Mărginean CO, Meliț LE, Mocan S, et al. An uncommon case of herpetic esophagitis in a small child with allergic rhinitis: A case report and literature review (CARE compliant) [J]. Medicine (Baltimore), 2019, 98(20): e15601
- [17] 申震, 李白芽, 戴浩, 等. 白细胞介素 27 在舌下脱敏治疗调控变应性鼻炎患者 Th17/Treg 平衡中的作用 [J]. 重庆医学, 2019, 48(3): 69-73
- [18] 王丰, 张虹婷, 孟娟. 皮下免疫与舌下免疫治疗变应性鼻炎的疗效比较[J]. 重庆医学, 2017, 46(21): 2906-2908
- [19] 杨贵, 邱书奇, 王鹏, 等. 儿童变应性鼻炎脱敏治疗前后生活质量对比研究[J]. 临床耳鼻咽喉头颈外科杂志, 2018(2): 95-98
- [20] 王任霞, 宁云红. 中药调理体质治疗中重度持续性变应性鼻炎的临床观察[J]. 中国中西医结合杂志, 2018, 38(09): 35-38
- [21] 闫占峰, 王璐璐, 巩政, 等. 鼻内针刺联合益气解敏汤治疗中重度变应性鼻炎肺脾气虚型 60 例临床观察[J]. 中医杂志, 2018, 59(12): 1035-1038
- [22] 许航宇, 舒海荣, 宋建新. 通窍鼻炎颗粒对中重度持续性变应性鼻炎患者的疗效及作用机制[J]. 中药材, 2017, 40(2): 485-487
- [23] 丁定明, 李思康, 张正龙, 等. 督脉灸治疗变应性鼻炎及对免疫功能的影响[J]. 针刺研究, 2016, 41(04): 338-342
- [24] 李泳文, 孙麦青. 玉屏风散联合督脉灸对变应性鼻炎患者血清 IL-6, cAMP, cGMP 的影响[J]. 中国实验方剂学杂志, 2018, 24(11): 163-167
- [25] 张茜. 香菊胶囊对变应性鼻炎患者 IgE、IL-4、IL-8 及 EOS 的影响 [J]. 海南医学院学报, 2016, 22(05): 490-492
- [26] 刘永平, 陈蕴光, 郑俊斌, 等. 变应性鼻炎鼻激发后鼻腔分泌物嗜酸性粒细胞增加与血清特异性 IgE 水平正相关[J]. 细胞与分子免疫学杂志, 2017, 33(1): 85-88
- [27] 颜征鸿, 周序军, 廖进, 等. 麻黄连翘赤小豆汤加减对肺经郁热型变应性鼻炎 Th1/Th2、Th17、Treg 细胞的影响[J]. 现代中西医结合杂志, 2018, 27(15): 1685-1688
- [28] 刘承耀, 王向东, 郑铭, 等. 鼻用糖皮质激素对变应性鼻炎和非变应性鼻炎患者鼻呼吸道一氧化氮浓度的影响[J]. 中国耳鼻咽喉头颈外科, 2018, 25(06): 309-314
- [29] Luo XQ, Ma F, Wang S, et al. Interleukin-5 induces apoptotic defects in CD4 $^{+}$ T cells of patients with allergic rhinitis [J]. J Leukoc Biol, 2019, 105(4): 719-727
- [30] 张俊清. 加味玉屏风干预变应性鼻炎的疗效及安全性系统评价[J]. 中国中医基础医学杂志, 2016, 22(01): 99-101