

doi: 10.13241/j.cnki.pmb.2021.03.013

玉屏风颗粒联合西咪替丁对过敏性紫癜患儿临床疗效及外周血免疫学指标的影响*

孙 靓¹ 黄 燕² 崔 晨³ 黄中迪⁴ 袁德利⁵

(上海中医药大学附属曙光医院 1 中药室; 2 检验科; 3 儿科; 4 血液科 上海 201203;

5 中国人民解放军北部战区总医院妇产科 辽宁 沈阳 110000)

摘要 目的:探讨玉屏风颗粒联合西咪替丁对过敏性紫癜患儿临床疗效及外周血免疫学指标的影响。**方法:**选取 2017 年 1 月至 2019 年 12 月我院 68 例过敏性紫癜患儿为研究对象,根据随机化原则将受试儿进行分组,其中对照组 34 例患儿仅接受西咪替丁治疗,研究组 45 例患儿在对照组的基础上口服玉屏风颗粒治疗,比较两组的治疗效果、治疗前后外周血免疫学指标水平变化及用药安全性。**结果:**研究组临床治疗总有效率显著高于对照组($P<0.05$),治疗前两组各免疫学指标及各炎性因子水平比较无统计学差异($P>0.05$),治疗后两组各免疫学指标及各炎性因子水平较治疗前均明显降低,且研究组显著低于对照组($P<0.05$),两组治疗期间不良反应发生率无差异($P>0.05$)。**结论:**玉屏风颗粒联合西咪替丁可有效改善患儿的临床症状及外周血免疫学指标,疗效安全显著,值得在过敏性紫癜患儿治疗中应用及推广。

关键词:玉屏风颗粒;西咪替丁;过敏性紫癜;免疫学指标;安全性

中图分类号:R544 文献标识码:A 文章编号:1673-6273(2021)03-467-04

Effect of Yupingfeng Granules Combined with Cimetidine on Clinical Efficacy and Peripheral Blood Immunological Parameters in Children with Allergic Purpura*

SUN Liang¹, HUANG Yan², CUI Chen³, HUANG Zhong-di⁴, YUAN De-li⁵

(1 Chinese Medicine Room, 2 Department of Laboratory Medicine, 3 Department of Pediatrics, 4 Department of Hematology, Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine, Shanghai, 201203, China;

5 Department of Obstetrics and Gynecology, General Hospital of the Northern Theater of the Chinese People's Liberation Army, Shenyang, Liaoning, 110000, China)

ABSTRACT Objective: To explore effect of Yupingfeng granules combined with cimetidine on clinical efficacy and peripheral blood immunological parameters in children with allergic purpura. **Methods:** 68 children with allergic purpura were selected as the subjects and conducted retrospective study from January 2017 to December 2019. The subjects were grouped according to the principle of randomization, the control group of 34 cases were treated with cimetidine, the study group of 34 cases on the basis of this combination of Yupingfeng granules. Therapeutic effect, changes in peripheral blood immunological indicators before and after treatment, and medication safety were compared the two groups. **Results:** The total effective rate of clinical treatment in the study group was significantly higher than that in the control group ($P<0.05$). There were no significant differences in immunological indexes and inflammatory factors levels between the two groups before treatment($P>0.05$). After treatment, the immunological indexes and inflammatory factors levels of the two groups were significantly lower than those before treatment, and the study group was significantly lower than the control group($P<0.05$). There was no significant difference in the incidence of adverse reactions between the two groups($P>0.05$). **Conclusion:** Yupingfeng granules combined with cimetidine can effectively improve the clinical symptoms and peripheral blood immunological indicators, and the effect is safe and significant. It is worthy of application and promotion in the treatment of children with allergic purpura.

Key words: Yupingfeng granules; Cimetidine; Allergic purpura; Immunological indicators; Safety

Chinese Library Classification(CLC): R544 **Document code:** A

Article ID: 1673-6273(2021)03-467-04

前言

过敏性紫癜(HSP)是临床上常见的一种系统性血管免疫

性疾病,又称自限性急性出血症,多由血管变应性炎症引起,使血管壁通透性及脆性增加,继而引发关节肿痛,皮肤及黏膜瘀点及瘀斑、肾炎、腹痛腹泻等一系列症候群,具有病情迁延不

* 基金项目:国家卫生计生委医药卫生科技发展研究中心项目(W2015CAE173)

作者简介:孙靓(1982-),女,本科,中药师,主要研究方向:中药学方向,电话:13916838416, E-mail: sjserina@126.com

(收稿日期:2020-04-06 接受日期:2020-04-30)

愈,易反复发作的特点,若未进行及时治疗,随着病情进展则会严重损害患儿的肾功能及免疫系统,甚至威胁到患儿的生命安全^[12]。针对过敏性紫癜临床上常采用抗感染、抗过敏、糖皮质激素、补充维生素 C 等药物联合西咪替丁来抗炎、抗变态反应、调节免疫,以改善患儿的临床症状,但治疗效果常不尽人意^[3,4]。中医认为,HSP 属于中医“紫斑”、“血证”范畴,采用玉屏风散治疗有助于扶正固本,提高机体免疫功能,进而改善临床症状,提高治疗效果^[5]。本研究选取 2017 年 1 月至 2019 年 12 月我院 68 例过敏性紫癜患儿为研究对象,探讨玉屏风颗粒联合西咪替丁对过敏性紫癜患儿临床疗效及对外周血免疫学指标的影响,以期临床提供参考。

1 资料与方法

1.1 一般资料

选取 2017 年 1 月至 2019 年 12 月我院 68 例过敏性紫癜患儿,根据随机化原则将受试儿进行分组,对照组:34 例患儿中男 20 例,女 14 例,年龄 4~15 岁,平均(9.24±2.12)岁,病程 2~18 d,平均(11.62±2.34)d,疾病类型:单纯型 10 例,腹型 8 例,关节型 6 例,混合型 6 例,肾型 4 例;研究组:34 例患儿中男 19 例,女 15 例,年龄 4~14 岁,平均(9.15±2.08)岁,病程 3~17 d,平均(11.55±2.42)d,疾病类型:单纯型 11 例,腹型 8 例,关节型 7 例,混合型 5 例,肾型 3 例。两组患儿的临床资料经统计学分析无显著差异性($P>0.05$),可进行数据对比。

1.2 纳入及排除标准

所有患儿均伴有不同程度的皮肤紫癜、关节肿痛、消化道症状等,经临床检查符合《诸福棠实用儿科学》中过敏性紫癜相关的诊断标准^[6],初次发病,家长知情同意,自愿参与本次研究,且排除既往严重的靶器官功能障碍、相关药物过敏史、风湿或感染性疾病、其他免疫系统疾病、治疗依从性差及临床资料不

全者。

1.3 方法

所有患儿入院后均卧床休息,给予补充维生素、抗感染、补液、抗过敏、糖皮质激素等常规治疗,对照组在此基础上给予 20 mg/(kg·d) 西咪替丁注射液(山东方明药业,国药准字 H37023309,规格:2 mL:0.2 g)静脉滴注,每日 2 次,连续治疗 2 w。研究组在对照组的基础上口服玉屏风颗粒(国药集团广东环球制药,国药准字 Z10930036,5 g/袋),每次 6~9 g,每日 2 次,连续治疗 2 w。比较两组的治疗效果、治疗前后外周血免疫学指标水平变化及用药安全性。

1.4 评价标准

(1)疗效评价标准^[7]:显效:治疗后皮肤紫癜、关节肿痛、消化道症状消失,实验室检各指标基本恢复正常;有效:治疗后症状明显改善,实验室指标明显好转;无效:治疗后症状均无明显好转或病情加重。(2)外周血免疫学指标:所有患者持续空腹 8 h 以上取静脉血 3 mL,采用 EDTA 抗凝处理后,应用免疫荧光法检测外周血中 CD4⁺、CD8⁺ 及 CD4⁺/CD8⁺ 水平^[8-11];另取肘静脉血 3 mL,离心分离出血清后采用免疫投射比浊法检测血清中 C3、IgG 及 IgM 水平,采用酶联免疫吸附法检测 IL-2、IL-6 及 IL-12 水平^[12-15]。

1.5 统计学方法

应用 SPSS 19.0 软件, $P<0.05$ 有统计学意义,计量资料采用($\bar{x} \pm s$)示,行 t 检验,计数资料采用(%)示,行 χ^2 检验。

2 结果

2.1 治疗效果

研究组临床治疗总有效率为 94.11%,显著高于对照组 79.41%($P<0.05$),见表 1。

表 1 治疗效果(例,%)

Table 1 Therapeutic effect(n, %)

Groups	Number	Excellent	Effective	Invalid	Total effective rate
Study Group	34	20(58.82)	12(35.29)	2(5.88)	32(94.11)*
Control group	34	17(50.00)	10(29.41)	7(20.59)	27(79.41)

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

2.2 治疗前后各免疫学指标变化

治疗前两组各免疫学指标比较均无统计学差异($P>0.05$),

治疗后两组各免疫学指标较治疗前均明显降低,且研究组更佳显著($P<0.05$),见表 2。

表 2 治疗前后各免疫学指标变化($\bar{x} \pm s$)

Table 2 Changes of immunological indexes before and after treatment($\bar{x} \pm s$)

Group	Cellular immune			The humoral immune			
	CD4 ⁺ (%)	CD8 ⁺ (%)	CD4 ⁺ /CD8 ⁺	CD4 ⁺ (%)	C3(g/L)	IgG(g/L)	IgM(g/L)
The study Group (n=34)	Before treatment	44.21± 2.38	35.72± 4.33	1.67± 0.31	3.68± 0.26	10.58± 2.26	7.69± 1.38
	After treatment	28.63± 3.02*#	28.42± 2.99*#	1.06± 0.30*#	1.22± 0.15*#	9.42± 1.75*#	1.29± 0.54*#
The control group(n=34)	Before treatment	43.75± 2.62	35.79± 4.67	1.65± 0.32	3.71± 0.28	10.62± 2.31	7.72± 1.41
	After treatment	35.46± 2.98*	31.55± 4.98*	1.21± 0.29*	1.96± 0.33*	10.11± 2.04*	2.61± 0.18*

Note: compared with before treatment and control group, * $P<0.05$, ** $P<0.05$.

2.3 治疗前后各炎性因子水平变化

组低于对照组($P<0.05$),见表3。

治疗后两组各炎性因子水平较治疗前均显著降低,且研究

表3 治疗前后各炎性因子水平变化($\bar{x} \pm s$, ng/L)

Table 3 Changes of levels of various inflammatory factors before and after treatment($\bar{x} \pm s$, ng/L)

Groups		IL-2	IL-6	IL-12
The study Group(n=34)	Before treatment	56.24 $\pm$ 6.88	68.53 $\pm$ 6.56	81.67 $\pm$ 9.37
	After treatment	20.38 $\pm$ 2.25**	23.34 $\pm$ 2.58**	40.12 $\pm$ 5.22**
The control group(n=34)	Before treatment	55.96 $\pm$ 6.73	69.07 $\pm$ 6.72	82.04 $\pm$ 9.22
	After treatment	32.42 $\pm$ 3.64*	34.82 $\pm$ 2.72*	52.63 $\pm$ 6.34*

Note: compared with before treatment and control group, * $P<0.05$, ** $P<0.05$.

2.4 安全性

治疗期间研究组发生腹泻1例,发热1例,头晕1例,不良反应发生率为8.82%,对照组患儿发生腹泻1例,发热1例,头晕2例,不良反应发生率为11.76%,两组比较无差异($P>0.05$)。

3 讨论

HSP是以广泛的小血管炎为病理基础的一种变态反应性出血性疾病,目前发病机制上尚不完全明确,但大多学者认为,HSP的病因与机体炎性反应、细胞因子水平及凝血机制有密切关系,病机主要为免疫调节功能异常、炎性递质异常、基因异常及凝血系统异常等^[16]。中医将HSP归于“斑毒”、“阴阳毒”、“血证”范畴,认为该病主要因风热毒邪入侵导致脉络损伤、邪热伤血、血液外溢所致,或因血热妄行、淤血,导致热淤伤及脏腑气血,身热面赤、肌肤紫斑等,或正气虚弱、气阴两虚所致,为虚实夹杂之证^[17]。

有研究指出,HSP患者体液免疫处于高反应状态,细胞免疫功能紊乱,其临床表现与抗原-抗体复合物反应有关^[18]。西咪替丁是一种组胺H₂受体拮抗剂,可有效抑制皮肤、血管及T细胞表面的H₂组胺受体来增加机体的免疫反应,提高T淋巴细胞转化率,减低小血管通透性,减轻对肾功能的损伤,同时还可抑制胃酸分泌,保护胃肠功能,进而缓解消化道症状^[19-23]。玉屏风颗粒是在玉屏风散的基础上由中药黄芪、炒白术、防风精制而成的一种中成药制剂,是中药“扶正固本”的经典方剂,益气固表、扶正祛邪作用显著^[24]。方中黄芪益气固表,止汗,白术健脾益气,可增强黄芪固表止汗之功,防风祛风散寒,诸药联合共奏祛邪而不伤正、固表不留邪之功效^[25-27]。现代药理研究表明,玉屏风颗粒可有效增强机体的免疫功能及肾上腺皮质功能,抑制机体对致敏物质发生病理免疫应答,抗变态反应、抗过敏作用显著。在西咪替丁的基础上联合应用可协同性的抑制机体免疫损伤及炎性反应,改善血管通透性,保护胃肠黏膜,促进病情康复^[28-30]。

本研究研究组临床治疗总有效率显著高于对照组,两组治疗期间不良反应发生率无差异,与姬爱华^[31]等学者的研究类似,该学者应用鲁司特片联合玉屏风颗粒治疗儿童过敏性紫癜,治疗后,试验组的有效率显著高于对照组(93.84% vs. 75.38%),且不增加药物不良反应的发生率,结果显示提示玉屏风颗粒可有效改善患儿临床症状,在提高治疗效果、促进病

情康复方面具有积极意义,且不增加不良反应,安全性较高。本研究结果也显示治疗前两组患者各免疫学指标及各炎性因子水平比较无统计学差异,治疗后两组各免疫学指标及各炎性因子水平较治疗前均明显降低,且研究组更低,与张迎涛^[32]等学者的研究一致,该学者研究发现玉屏风颗粒联合西药治疗过敏性紫癜小儿后,炎性因子指标(IL-2、6、12)均显著降低;同时学者牛文忠^[33]的研究结果也显示玉屏风颗粒联合常规治疗后患儿的免疫学指标均降低,说明玉屏风颗粒联合西咪替丁可协同性的发挥免疫调节作用,减轻炎性损伤,达到抗细菌感染的作用。本研究将玉屏风颗粒与西咪替丁治疗过敏性紫癜患儿,取得了一定的成效,可以为后续研究过敏性紫癜患儿的治疗提供方向。

综上所述,玉屏风颗粒联合西咪替丁可有效改善患儿的临床症状及外周血免疫学指标,疗效显著且安全,值得在过敏性紫癜患儿治疗中推广应用。本研究也有一定的不足,患儿样本量少,也没有对治疗机制进行深入探究。后续研究中,需要扩大样本量深入的探究玉屏风颗粒联合西咪替丁治疗过敏性紫癜的机制。

参考文献(References)

- [1] Shang Y, Yang CS, Cui huailiang, et al. Efficacy of azithromycin combined with methylamylon in the treatment of allergic purpura induced by mycoplasma pneumoniae infection [J]. Chin J Hospital Infection, 2019, 29(14): 224-2227
- [2] Goel S, DeCristo MJ, Watt AC, et al. CDK4/6 inhibition triggers anti-tumour immunity[J]. Nature, 2017, 548(7668): 471-475
- [3] Ren XM, Jia XH, Zhang YJ, et al. Clinical efficacy of vitamin E in the treatment of allergic purpura and its effect on inflammatory factors[J]. International J Immunology, 2018, 41(1): 37-40
- [4] Edward S Taylor, John L McCall, Shirley Shen, et al. Prognostic roles for IL-2-producing and CD69⁺T cell subsets in colorectal cancer patients: IL-2 in colorectal cancer patients [J]. Internat J Cancer, 2018, 143(8): 329-331
- [5] Ji AH, Peng ZJ. Clinical study on the treatment of allergic purpura with monroost tablets and yupingfeng granule [J]. Chinese J Clin Pharmacol, 2017, 33(17): 1644-1646
- [6] Hu YM, Jiang ZF. Practical pediatrics [M]. 7th Ed.Beijing: people's medical publishing house, 2002
- [7] Shearer GM, Clerici M. In vitro analysis of cell-mediated immunity: clinical relevance[J]. Clinical Chemistry, 2020, (11): e11

- [8] Qingliang Zheng, Jin Hou, Ye Zhou, et al. The RNA helicase DDX46 inhibits innate immunity by entrapping m(6)A-demethylated antiviral transcripts in the nucleus [J]. Science Foundation in China, 2017, 18 (4): 1094-1103
- [9] Qingzhu Zhang, Huaxiang Yin, Lingkuan Meng, et al. Novel GAA Si Nanowire p-MOSFETs with Excellent Short Channel Effect Immunity by Advanced Forming Process [J]. IEEE Electron Device Letters, 2018, 39(4): E464
- [10] Wei Yin, Yan Song, Qing Liu, et al. Topical treatment of All-trans Retinoic Acid inhibits murine melanoma partly by promoting CD8(+) T cell immunity[J]. Immunology, 2017, 152(2): 438-440
- [11] Gopalakrishnan, Vancheswaran, Helmink, et al. The Influence of the Gut Microbiome on Cancer, Immunity, and Cancer Immunotherapy [J]. Cancer Cell, 2018, 33(4): 570-580
- [12] Longlong Yang, Lingying Liu, Huinan Ying, et al. Acute downregulation of miR-155 leads to a reduced collagen synthesis through attenuating macrophages inflammatory factor secretion by targeting SHIP1 [J]. J Molecular Histology, 2018, 49(1): 1-10
- [13] Joo HK, Choi S, Yu RL, et al. Ethanol Extract of Brassica rapa ssp. pekinensis Suppresses Tumor Necrosis Factor- α -Induced Inflammatory Response in Human Umbilical Vein Endothelial Cells [J]. J Med Food, 2017, 20(5): 511-518
- [14] Samir M, Glistler C, Mattar D, et al. Follicular expression of pro-inflammatory cytokines tumour necrosis factor- α (TNF α), interleukin 6 (IL6) and their receptors in cattle: TNF α , IL6 and macrophages suppress thecal androgen production in vitro [J]. Reproduction, 2017, 32 (17): 35-49
- [15] Kamimura T, Isobe N, Yoshimura Y. Effects of inhibitors of transcription factors, nuclear factor- κ B and activator protein 1, on the expression of proinflammatory cytokines and chemokines induced by stimulation with Toll-like receptor ligands in hen vaginal cells [J]. Poultry Science, 2017, 96(3): 723-730
- [16] Guo QY, DingY, Song CD, et al. Clinical analysis of 16 cases of allergic purpura complicated with surgical complications in children[J]. J Anhui Med, 2019, 23(8): 1526-1528
- [17] Zsolt Czimmerer, Bence Daniel, Attila Horvath, et al. The Transcription Factor STAT6 Mediates Direct Repression of Inflammatory Enhancers and Limits Activation of Alternatively Polarized Macrophages[J]. Immunity, 2018, 48(1): 75-90
- [18] Sun Y, Hu XW, Tang HN, et al. Effects of hydrocortisone combined with cimetidine on peripheral blood T lymphocyte subsets and serum sscam-1 levels in patients with allergic purpura [J]. Chinese J Endemic Disease Control Prevention, 2017, 32(9): 1075-1078
- [19] Alison Hogg, Yongjun Sui, Shlomo Z. Benlogasson, et al. Role of CD4 T cell helper subsets in immune response and deviation of CD8 T cells in mice[J]. European J Immunol, 2017, 47(12): 765-767
- [20] Cretella D, Ravelli A, Fumarola C, et al. The anti-tumor efficacy of CDK4/6 inhibition is enhanced by the combination with PI3K/AKT/mTOR inhibitors through impairment of glucose metabolism in TNBC cells [J]. J Exp Clin Cancer Res, 2018, 37(1): E72
- [21] Janko Nikolich-Zugich. The twilight of immunity: emerging concepts in aging of the immune system [J]. Nature Immunology, 2017, 19(1): 10-19
- [22] Fang Y, Suveena Sharma, Dragana Jankovic, et al. The transcription factor Bhlhe40 is a switch of inflammatory versus antiinflammatory Th1 cell fate determination [J]. J Experimental Med, 2018, 215(7): 1813-1821
- [23] Weng MT, Park SH, Matsuoka K, et al. Incidence and Risk Factor Analysis of Thromboembolic Events in East Asian Patients With Inflammatory Bowel Disease, a Multinational Collaborative Study [J]. Inflamm Bowel Dis, 2018, 24(8): 1791-1800
- [24] 高宇, 沈朝斌, 周霖, 等. 玉屏风颗粒对急性发作期哮喘患儿 H4R 表达的影响[J]. 安徽医药, 2018, 22(2): 335-338
- [25] 廖小芳, 毕晓黎, 胥爱丽, 等. UPLC 法同时测定玉屏风颗粒中 9 种成分[J]. 中成药, 2019, 41(8): 1778-1781
- [26] 张圆圆, 汤建萍, 罗勇奇, 等. 玉屏风颗粒对牛奶蛋白过敏患儿 Th17/Treg 平衡的影响[J]. 中国医师杂志, 2018, 20(8): 1171-1175
- [27] Jayla Gray, Arielle Gray, James Swan, et al. Perianal extramammary Paget disease treated with topical imiquimod and oral cimetidine[J]. Cutis, 2018, 101(4): E19
- [28] Ghada Ben Youssef, Marie Tourret, Marion Salou, et al. Ontogeny of human mucosal-associated invariant T cells and related T cell subsets [J]. J Exp Med, 2018, 215(2): 459-479
- [29] Devinder Toor, Neha Sharma. T cell subsets: an integral component in pathogenesis of rheumatic heart disease[J]. Immunol Res, 2017, 66 (9480): 1-13
- [30] Anders Dige, Maria K. Magnusson, Claus Uhrenholt, et al. Effects of Anti-TNF α Treatment on Mucosal Expression of IL-17A, IL-21, and IL-22 and Cytokine-Producing T Cell Subsets in Crohn's Disease[J]. Med Inflamm, 2018, 2018(3): 1-7
- [31] 姬爱华, 彭振居. 孟鲁司特片联合玉屏风颗粒治疗过敏性紫癜的临床研究[J]. 中国临床药理学杂志, 2017, 33(17): 1644-1646
- [32] 张迎涛, 魏平平. 孟鲁司特钠联合玉屏风颗粒治疗小儿过敏性紫癜的疗效评价[J]. 中国社区医师, 2019, 35(11): 111+113
- [33] 牛文忠, 张雪松, 丁显春. 玉屏风散对过敏性紫癜患儿免疫调节作用的影响[J]. 中国皮肤性病学杂志, 2017, 31(9): 91-93