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白芍总苷对糜烂型口腔扁平苔藓外周血 TNF-α,IFN-γ 及 IL-10 水平的影响 *

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摘要 目的:研究白芍总苷对糜烂型口腔扁平苔藓外周血肿瘤坏死因子(TNF-α)、γ- 干扰素(IFN-γ)及白细胞介素 -10(IL-10)水平的影响。**方法:**选取 2014 年 7 月至 2015 年 7 月我院接诊的糜烂型口腔扁平苔藓患者 80 例作为本次研究对象。对照组患者采用低浓度他克莫司治疗,观察组采用白芍总苷治疗,观察两组患者治疗前后血清 TNF-α、IFN-γ 及 IL-10 水平的变化、糜烂面积、疼痛评分及近期治疗疗效。**结果:**治疗后,观察组血清 TNF-α、IL-10 水平显著低于对照组,血清 IFN-γ 水平明显高于对照组[(2.16± 0.61)μg/mL vs(3.04± 0.80)μg/mL、(258.93± 5.72)ng/L vs(273.41± 6.03)ng/L、(319.27± 53.46)ng/L vs(290.95± 51.03)ng/L(P＜0.05),糜烂面积、疼痛评分均显著低于对照组[(0.10± 0.03)cm^2 vs(0.51± 0.10)cm^2、(1.01± 0.30)分 vs(3.20± 0.78)分](P＜0.05),近期治疗疗效优于对照组 95.00%(38/40)vs75.00%(30/40)(P＜0.05)。**结论:**白芍总苷治疗糜烂型口腔扁平苔藓的效果显著,可能与其调节血清 TNF-α、IFN-γ 及 IL-10 的水平有关。

关键词:白芍总苷;糜烂型口腔扁平苔藓;肿瘤坏死因 q 子(TNF-α);γ- 干扰素(IFN-γ);白细胞介素 -10(IL-10)

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Effect of Total Glucosides of Paeony on the TNF-α, IFN-γ and IL-10 Levels in the Peripheral Blood of patients with Erosive Oral Lichen Planus*

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ABSTRACT Objective: To study the effect of total glucosides of paeony on the serum tumor necrosis factor (TNF-α), Interferon-γ (IFN-γ) and interleukin-10 (IL-10) levels of patients with erosive oral lichen planus. **Methods:** 80 patients of erosive oral lichen planus who were treated from March 2014 to March 2015 in our hospital were selected as the research objects. The control group was treated with Low concentration tacrolimus, while the observation group was treated with Total glucosides of paeony, Then the Changes of IL-10, IFN- and TNF-α, erosion area, pain score before and after, the short-term therapeutic effect were compared. **Results:** After treatment, the serum TNF-α, IL-10 levels in the Observation group were lower than those of the control group, the seum IFN-γ level was higher than those of the control group[(2.16± 0.61)μg/mL vs(3.04± 0.80)μg/mL, (258.93± 5.72)ng/L vs(273.41± 6.03)ng/L, (319.27± 53.46)ng/L vs(290.95± 51.03)ng/L(P＜0.05); the erosion area, pain score of the Observation group were less than those of the control group[(0.10± 0.03)cm^2 vs(0.51± 0.10)cm^2, (1.01± 0.30)score vs(3.20± 0.78)score](P＜0.05), the short-term effective rate of observation group was statistically higher than that of the control group [95.00%(38/40)vs75.00%(30/40)(P＜0.05). **Conclusion:** Total glucosides of paeony was well for the erosive oral lichen planus, which could regulate the serum TNF-α, IFN-γ and IL-10 level and had im- munomodulatory effects.

Key words: Total glucosides of paeony; Erosive oral lichen planus; TNF-α; IFN-γ; IL-10

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前言

糜烂型口腔扁平苔藓在临床较为多见,常在充血的基础上发生糜烂,临床症状主要为口腔粘膜出现白色的花纹,主要发生于颊、唇、前庭沟、磨牙后区、舌腹等部位,疼痛较明显,对患者的生活造成较大的影响[1,2]。若不及时治愈,患者的临床症状不会得到改善,甚至会出现恶化。该病具有病情复杂、发病反复的特点,随着病程的延长,患者的症状也会随之加重,因此应及时采取正确有效的治疗方法[3]。近年来研究显示糜烂型口腔扁平苔藓发生与免疫功能失调有关。本研究主要探讨了白芍总苷对糜烂型口腔扁平苔藓外周血 TNF-α、IFN-γ 及 IL-10 的影响。现报道如下。

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1 资料与方法

1.1 一般资料

选取 2014 年 7 月至 2015 年 7 月我院接诊的糜烂型口腔扁平苔藓患者 80 例作为本次研究对象。纳入标准[4]:① 均符合糜烂型口腔扁平苔藓;② 近期未使用抗生素及消炎药;③ 肝脏功能正常;④ 同意本次研究患者;排除标准:① 患有糖尿病、高血压、心脑血管疾病患者;② 妊娠及哺乳期患者;③ 对治疗药物过敏患者;④ 患有精神疾病。按照随机数表法分为观察组和对照组,观察组 40 例,男 23 例,女 17 例,年龄 25~70 岁,平均年龄(46.38± 3.27)岁,病程 1~19 个月,平均病程(11.07± 1.01)月;对照组 40 例,男 22 例,女 18 例,年龄 25~72 岁,平均年龄(47.85± 3.76)岁,病程 1~18 个月,平均病程(11.12± 1.19)月。本研究已通过伦理委员会批准,两组患者的年龄、性别、病程等一般临床资料比较差别均无统计学意义(P＞0.05),具有可比性。

1.2 治疗方法

对照组患者采用低浓度他克莫司(规格:40 mL;生产厂家:安斯泰来制药(中国)有限公司;批号 20160519)进行治疗,将棉签涂抹上 0.1%他克莫司软膏后,然后涂抹在患者的颊黏膜糜烂病变处,上药后,1 小时之内勿漱口,勿进食、勿吞入,每天 2 次,共治疗 2 个月。

观察组患者在对照组的基础上加用白芍总苷胶囊 (规格:0.3 g;生产厂家:宁波立华制药有限公司;批号:20140429)进行治疗,每次 0.6 g,每日 3 次,勾起嚼服,饭前服用,每次 15 g·d^{-1},每天 1 次,共治疗 2 个月。

1.3 观察指标

观察两组患者治疗前后血清 TNF-α、IFN-γ 及 IL-10 水平的变化,糜烂面积,疼痛评分,近期治疗疗效。血清 TNF-α、IFN-γ 及 IL-10 的检测方法:分别采集两组患者治疗前后清晨空腹静脉血 5 mL,进行 3000 r/min、离心 15 min 分离血清,取上层血清,将其放置于 -80℃进行等待检测,采用由上海邦奕生物专业供应的酶联免疫吸附试剂盒进行测定。采用疼痛状况评分标准:无痛(0 分);轻度(1~3 分);中度(4~6 分);重度(7~10分)。

1.4 疗效评定标准[5]

疼痛完全消失,充血、糜烂、白色条纹等临床体征完全消失为显效;疼痛等临床症状减轻,充血、糜烂、白色条纹等的面积缩小为有效;临床症状未减轻或加重为无效。

1.5 统计学分析

所有数据采用 SPSS18.0 统计学软件进行分析处理,计数资料采用卡方检验,计量资料采用 t 检验,以 P＜0.05 为差异有统计学意义。

2 结果

2.1 两组患者治疗前后血清 TNF-α、IFN-γ 及 IL-10 水平的比较

治疗前,两组患者血清 TNF-α、IFN-γ、IL-10 水平比较差异无统计学意义(P＞0.05)。治疗后,两组患者血清 TNF-α、IL-10 水平均上升,IFN-γ 水平下降,观察组血清 TNF-α、IFN-γ、IL-10 水平较治疗前差异具有统计学意义(P＜0.05),对照组 IFN-γ 较治疗前差异无统计学意义(P＞0.05),观察组血清 TNF-α、IL-10 水平小于对照组,血清 IFN-γ 水平高于对照组(P＜0.05),见表1。

表 1 两组患者治疗前后血清 TNF-α、IFN-γ 及 IL-10 水平比较($\bar{x}$± s)

Table 1 Comparison of the serum TNF-α, IFN-γ and IL-10 levels between the two groups before and after treatment ($\bar{x}$± s)

Groups		TNF-α(μg/mL)	IFN-γ(ng/L)	IL-10(ng/L)
Observation group(n=40)	Before treatment	4.18± 1.02	283.67± 51.02	298.37± 7.03
	After treatment	2.16± 0.61*#	319.27± 53.46*#	258.93± 5.72*#
Control group(n=40)	Before treatment	4.20± 1.03	282.28± 50.90	297.29± 6.39
	After treatment	3.04± 0.80*	290.95± 51.03	273.41± 6.03*

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

2.2 两组患者治疗前后糜烂面积和疼痛评分比较

治疗前,两组患者糜烂面积和疼痛评分比较差异无统计学意义(P＞0.05)。治疗后,两组患者糜烂面积和疼痛评分均较治疗前显著下降(P＜0.05),且观察组糜烂面积、疼痛评分均明显小于对照组(P＜0.05),见表 2。

表 2 两组患者治疗前后糜烂面积和疼痛评分比较($\bar{x}$± s)

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

Groups		Erosion area(cm^2)	Pain score(分)
Observation group(n=40)	Before treatment	0.91± 0.23	8.35± 1.20
	After treatment	0.10± 0.03*#	1.01± 0.30*#
Control group(n=40)	Before treatment	0.93± 0.22	8.36± 1.23
	After treatment	0.51± 0.10*	3.20± 0.78*

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

2.3 两组患者近期疗效比较

观察组近期治疗总有效率为 95%,明显高于对照组 (P＜0.05),见表 3。

表 3 两组患者近期治疗疗效比较[例(%)]

Table 3 Comparison of the short-term therapeutic effects between two groups of patients[n(%)]

Groups	Cure	Effective	Invalid	Total effective rate
Observation group(n=40)	30(75.00)	8(20.00)	2(5.00)	38(95.00)#
Control group(n=40)	24(60.00)	6(15.00)	10(25.00)	30(75.00)

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

3 讨论

目前,口腔扁平苔藓是一种慢性炎症性疾病,发病机制尚不完全明确,但有研究认为该病与精神因素、免疫因素、内分泌因素、感染因素等均有关[5]。值得注意的是,糜烂型口腔扁平苔藓已被 WHO 列入口腔癌前状态,其比糜烂型口腔扁平苔藓更容易反复发作,非常出现剥脱糜烂,自发痛明显,有时伴有假膜形成,对患者的生活及健康造成影响[6,7]。

白芍总苷是一种从白芍干燥根中生化提取的多种具有生理功效成分的混合物,具有调节免疫功能。此外,白芍具有养血柔肝、缓中止痛、敛阴收汗的作用[18,19]。本研究中,采用白芍总苷治疗的患者治疗后糜烂面积和疼痛评分均低于采用低浓度他克莫司治疗的患者,治疗总有效率为 95.00%,而采用低浓度他克莫司治疗的患者总有效率为 75.00%。这表明白芍总苷能够有效提高口腔扁平苔藓的疗效。

近年来,有研究表明免疫因素是糜烂型口腔扁平苔藓的发病机制中的主要原因[8]。Th1、Th2、Th17 是 CD4T 辅助细胞的三个细胞亚群,在正常的情况下 Th1、Th2 处于平衡状态,但 Th1、Th2 细胞在患者机体内的免疫和疾病的发展中所起到的作用是完全不同的[9]。Th1 细胞主要是介导细胞毒和机体局部炎症有关的免疫应答,分泌 IFN-γ 为代表的细胞因子[10]。与患者器官特异性自身免疫病、慢性炎症、接触性皮炎、一直排斥、迟发性超敏反应有关 [11]。在 Th2 细胞中,IL-4、IL-10 是主要分泌因子,主要为对抗细胞外多细胞寄生虫的免疫反应,可刺激机体 B 细胞的增殖[12]。IFN-γ 具有 Th1 细胞分化和抑制 Th2 细胞的功效,具有使 Th1 和 Th2 细胞亚群达到平衡状态的作用,还具有抗病毒、抗增殖活性以及有效杀伤细胞、巨噬细胞、T 淋巴细胞作用, 已在临床上关于口腔扁平苔藓探讨中得到多次研究[13,14]。IL-10 由 Th1 细胞分化,其具有抗炎作用,可抑制嗜酸粒细胞,并且能够使其加速凋亡,具有抗过敏效应[15]。可抑制 $CD4^+$T 细胞活化,糜烂型口腔扁平苔藓外周血中 IL-10 水平的表达与其病因有重要的相关性[16]。TNF-α 能够激活单核巨噬细胞分泌,可促进 T 细胞产生各种炎症因子及炎症反应[17]。

有研究表明白芍总苷具有双向调节作用,能够通过作用于机体多个环节来影响机体免疫功能, 且具有一定的药物依耐性,不会对患者的肝肾功能造成影响,仅见患者大便次数增多,安全可靠[20]。在本研究中,采用白芍总苷治疗的患者 TNF-α、IL-10 小于采用低浓度他克莫司治疗的患者,IFN-γ 高于采用低浓度他克莫司治疗的患者,提示其可抑制口腔扁平苔藓时的炎症反应, 这可能是其提高口腔扁平苔藓临床疗效的作用机制之一。

综上所述,白芍总苷治疗糜烂型口腔扁平苔藓具有良好的效果,能够调节外周血 TNF-α、IFN-γ 及 IL-10 的水平。

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