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清热散结片联合阿维A胶囊治疗难治性银屑病的疗效及对炎症反应的影响

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摘要 目的：分析清热散结片联合阿维A胶囊治疗难治性银屑病的疗效，并探讨其对炎症反应的影响。**方法**：选择2013年3月-2016年3月我院收治的100例难治性银屑病患者作为研究对象，按照随机数字表法分为对照组和观察组，每组各50例；对照组给予口服阿维A胶囊，观察组在对照组的基础上给予口服清热散结片；对比两组的临床疗效及不良反应发生情况，检测治疗前后血清肿瘤坏死因子(TNF-α)、白细胞介素-8(IL-8)及白细胞介素-4(IL-4)水平变化。**结果**：观察组的总有效率为96.00%(48/50)，显著高于对照组的84.00%(42/50)，差异有统计学意义(P<0.05)；治疗前两组TNF-α、IL-8及IL-4的水平对比，差异无统计学意义(P>0.05)，治疗后两组TNF-α、IL-8及IL-4水平均有所降低，且观察组显著低于对照组，差异有统计学意义(P<0.05)；治疗期间，两组无严重不良反应，差异无统计学意义(P>0.05)。**结论**：清热散结片联合阿维A胶囊治疗难治性银屑病的疗效显著，能够明显缓解患者机体的炎性反应，值得临床推广应用。

关键词：清热散结片；阿维A胶囊；难治性银屑病；疗效

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Efficacy of Heat Fights Piece combine with Avi A Capsule in The Treatment of Intractable Psoriasis and Its Influence on The Inflammatory Response

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ABSTRACT Objective: Efficacy of Heat Fights Piece combine with Avi A Capsule in The Treatment of Intractable Psoriasis and Its Influence on The Inflammatory Response, and to explore its effect on the inflammatory response. **Methods:** Selected 100 cases of patients with refractory psoriasis who were treated in our hospital from March 2013 to March 2016, and divided them into control group and observation group according to random number table method 50 cases in each group; Control group given oral avi A capsule, on the basis of the control group ,the observation group were given oral heat fights combine with avi A capsule; Compared two groups of clinical curative effect and adverse reactions occur, changes of serum tumor necrosis factor (TNF-α), interleukin 8 (IL-8) and interleukin 4 (IL-4) level were tested before and after treatment. **Results:** Observation group total effective rate was 96.00% (48/50), significantly higher than that of control group 84.00% (42/50), the difference was statistically significant (P<0.05); The two groups before treatment TNF-α, IL-8 and the levels of IL-4 contrast, there was no statistically significant difference (P>0.05), the two groups after treatment TNF-α, IL-8 and IL-4 levels are reduced, and the observation group was significantly lower than the control group, the difference was statistically significant (P<0.05); During the treatment, no serious adverse reaction in both groups, there was no statistically significant difference(P>0.05). **Conclusion:** Combination of heat fights piece and avi A capsule in the treatment of refractory psoriasis can significantly alleviate inflammatory reaction of the patients body and improve the treatment effect, and it worthy of clinical application.

Key words: Heat fights; Enjoying A capsule; Refractory psoriasis; The curative effect

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前言

银屑病为慢性复发性炎症性皮肤病，俗称"牛皮藓"，有寻常型和难治性之分，难治性包括关节病型、红皮病型以及脓疱型等，其特点为皮损广泛、久治不愈、反复发作以及病情危重。据流行病学调查统计结果显示，在欧洲该病的发病率高达2.9%，而在亚洲相对较低，基本处于1%以下[1]，我国相关资料显示自1984年-2008年以来，难治性银屑病的发病率已从0.123%逐渐上升至0.47%，上升趋势十分明显[2]。难治性银屑病不但会损害人体重要脏器，随着病情的进展会导致免疫系统功能下降，继而引发多种并发症危及患者的生命。常规治疗方法多使用糖皮质激素类药物，但是治疗效果较差。本研究以100例难治性银屑病患者为例，分析清热散结片联合阿维A胶囊治疗难治性银屑病的疗效，并探讨其对炎症反应的影响。现报道如下：

1 资料与方法

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1.1 一般资料

选择 2013 年 3 月 -2016 年 3 月我院收治的 100 例难治性银屑病患者。纳入标准:(1)所有患者均符合顾伟程编著的《精编皮肤病学》中关于银屑病的诊断标准[3],皮损面积在体表面积的 30%以上者;(2)接受 2 种及以上常规药物治疗,且治疗效果不甚理想者;(3)年龄介于 19-75 岁之间者。排除标准:(1)排除有明显感染患者;(2) 伴自身免疫病或代谢性疾病和内分泌系统性疾病者;(3)查体见肝肾功能不全者;(4)处于妊娠期、哺乳期者;(5)对清热散结片和阿维 A 胶囊等药物过敏者;(6)有重症光敏感病史者;(7)半年内使用维甲酸、免疫抑制或糖皮质激素等药物治疗者。按照随机数字表法分为对照组和观察组,每组各 50 例;其中,对照组男性 29 例,女性 21 例;年龄 19-75 岁,平均年龄(42.3± 9.5)岁,平均病程为(6.8± 4.5)年。观察组男性 30 例,女性 20 例;年龄 18-75 岁,平均年龄(43.1± 8.8)岁;平均病程为(7.0± 3.4)年。两组患者一般资料比较无显著差异(P>0.05),具有可比性。本次研究患者均自愿签署知情同意书,且经医院伦理委员批准通过。

1.2 方法

1.2.1 治疗方法 所有患者均于患处涂擦安抚剂和润肤霜。对照组给予口服阿维 A 胶囊(商品名称:方希;国药准字:H20010126;规格:10 mg× 10 s× 3 板;生产企业:重庆华邦制药有限公司),30 mg/ 次,1 次 /d,持续一周,一周后增至 30-50 mg/ 次;观察组在对照组的基础上给予口服清热散结片(商品名称:白云山;国药准字:Z44022794;规格:0.33 g× 48 s;生产企业:广州白云山奇星药业有限公司),5-8 片 / 次,3 次 /d,1 个月为 1 疗程,两组患者均连续治疗 3 个月。

1.2.2 血清指标采集 治疗前后,于空腹 12 h 后,采集 5 mL 静脉血,并选择 2-16N 高速离心机(湖南恒诺仪器设备有限公司)进行血清分离,选择 HBS-1096B 酶标仪(南京德铁实验设备有限公司),并根据试剂盒说明书操作,按照酶联免疫吸附法(Enzyme linked immunosorbent assay, ELISA)检测血清内白细胞介素 4(Interleukin-4, IL-4)、白细胞介素 8(Interleukin-8IL-8)以及肿瘤坏死因子 α(Tumor Necrosis Factor α, TNF-α)等指标水平(注:以上血清指标均在华中科技大学协和医院进修期间进行检测)。

1.3 观察指标及疗效评价

记录两组患者的治疗总有效率、不良反应发生率,以及治疗前后两组患者各炎性因子的变化情况。

按照皮损面积与严重程度指数(Psoriasis area and severity index, PASI)对患者的疗效进行评价[4];(1)治愈:皮损面积和治疗前对比缩小程度在 95%以上,PASI 评分(与治疗前对比)减少程度在 90%以上;(2)显效:皮损面积缩小程度在 75%-95%之间,PASI 评分减少程度在 60%-90%之间;(3)有效:皮损面积缩小程度在 25%-75%之间,PASI 评分减少程度在 20%-60%之间;(4)无效:皮损面积缩小程度在 25%以下,PASI 评分减少程度在 20%以下。总有效率 = [(治愈 + 显效 + 有效)/ 总例数]× 100%。

1.4 统计学方法

采用 SPSS20.0 统计学软件处理,计量资料以($\bar{x}$± s)表示,采用配对 t 检验;计数资料以百分率(%)表示,行(x^2)检验比较,P<0.05 时,差异有统计学意义。

2 结果

2.1 两组临床疗效

观察组的总有效率为 96.00%(48/50),显著高于对照组的 84.00%(42/50),差异有统计学意义(P<0.05),详见表 1。

表 1 两组临床疗效对比[n(%)]

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

Groups	Cure	Effective	Effective	Invalid	Total effective rate
Control group	7(14.00)	15(30.00)	20(40.00)	8(16.00)	42(84.00)
Observation group	12(24.00)	24(48.00)	12(24.00)	2(4.00)	48(96.00)
X^2					4.000
P					0.037

2.2 治疗前后两组 TNF-α、IL-8 及 IL-4 水平

治疗前两组 TNF-α、IL-8 及 IL-4 水平无显著差异(P>0.05);治疗后各项指标均有所降低,且观察组显著低于对照组,差异有统计学意义(P<0.05),详见表 2。

表 2 两组患者治疗前后 TNF-α、IL-8 以及 IL-4 水平对比[$\bar{x}$± s]

Table 2 Comparison of TNF-α, IL-8 and IL-4 levels between the two groups before and after treatment[$\bar{x}$± s]

Groups		TNF-α(ng/mL)	IL-8(pg/mL)	IL-4(pg/mL)
Control group	Before treatment	2.56± 0.35	74.33± 10.25	45.42± 6.12
	After treatment	1.47± 0.21*	49.66± 7.08*	26.44± 3.72*
Observation group	Before treatment	2.44± 0.34	74.76± 10.66	45.35± 6.42
	After treatment	0.91± 0.13*#	41.87± 5.36*#	16.54± 2.31*#

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

2.3 两组患者不良反应发生率对比

治疗期间,观察组出现 1 例皮肤干燥,2 例光过敏症状,0 例甲沟炎,不良反应发生率为 6.00%(3/50);对照组不良反应发生率为 10.00%(5/50),两组不良反应发生率对比,无显著差异

(P>0.05),详见表 3。

表 3 两组患者不良反应发生率对比 [n(%)]

Table 3 Comparison of the incidence of adverse reactions in two groups [n(%)]

Groups	N	Xerosis cutis	Light allergic	Paronychia	Incidence of adverse reactions
Control group	50	2(4.00)	1(2.00)	2(4.00)	10.00
Observation group		1(2.00)	2(4.00)	0	6.00
X^2		-	-	-	1.240
P		-	-	-	>0.05

3 讨论

银屑病的致病因是多方面的,如遗传、病毒感染、药物作用、情绪应激反应以及环境影响等,目前银屑病的病因尚未完全明确,给治疗带来巨大阻碍[5-7]。难治性银屑病是银屑病发展至最严重的阶段,其特点为久治难愈、皮损严重,给患者的日常工作和生活质量造成很大影响。传统中医理论认为,银屑病属于"白疕"、"松皮癣"等范畴,主因风热、风燥等邪物侵袭机体之内,肌肤郁热,热入血络,病久不愈,久病入络,毒损络脉发为难治性银屑病,因此治疗的原则为清热、解毒、通络[8,9]。西医的治疗原则即通过药物来调控基因,诱导病变细胞趋于凋亡并控制细胞的异常增长,逐渐使得上皮细胞恢复正常的生长、代谢状态,恢复细胞免疫能力抑制炎症反应。中医医内,西医治外,两种方法相结合从而提升治疗的效果。

阿维 A 胶囊作为主治严重银屑病的常用药物,其机理为促进表皮细胞增殖、分化,抑制皮肤异常角化,并缩小皮损面积,从而达到缓解病情的目的[10,11]。而清热散结片为纯中药制剂,具有消炎解毒、散结止痛之功效,其主要成分为千里光。千里光属于菊科植物千里光的全草,味苦、性寒,内含大量的毛茛黄素(flavoxanthin)、菊黄质(Chrysanthemaxanthin),及少量的 β-胡萝卜素(β-carotene);还含千里光宁碱(senecionine),千里光菲灵碱(seneciphylline)及氢酯(hydroquinone),对-羟基苯乙酸(p-hydroxyphenylaceticacid),香草酸(vanillic acid),水杨酸(salicylic acid),焦粘酸(pyromucic acid),针对皮炎湿疹等常见皮肤病疗效显著[12-14]。其中毛茛黄素在临床上主要应用于清热解毒,凉血消肿;β-胡萝卜素属于抗氧化剂,具有解毒作用,同时可增进血液循环,促使皮肤细嫩光滑,肤色红润,对美容健肤具有独到作用,适宜皮肤干燥、粗糙,或患毛发苔藓、黑头粉刺等皮肤病患者[15,16]。本研究对照组仅使用阿维 A 胶囊进行治疗,观察组则在对照组的基础上加用清热散结片进行治疗,结果显示:观察组总有效率为 96.00%(48/50),显著高于对照组的 84.00%(42/50),差异有统计学意义(P<0.05),与 Prieto-Pérez R[17] 研究结果基本保持一致。

同时,我们实时测定两组患者血清中 TNF-α、IL-4 和 IL-8 的含量变化,该 3 种物质均为常见的炎症因子。对于银屑病患者而其 T 淋巴细胞被激活后会大量分泌炎症因子,因此该 3 种物质的含量均明显升高,医学研究发现,IL-8 细胞因子是导致脓包型银屑病产生的重要因素,IL-4 的作用是抑制机体免疫能力,导致 Th0 分化为 Th2 促使淋巴细胞快速增值从而加重病情[18,19]。两组患者在治疗后 3 种炎症因子含量均明显下降,且观察组显著优于对照组,差异有统计学意义(P<0.05),此外,两组不良反应发生率无统计学差异。据此可见,两种药物联合使用疗效更为确切,且无严重不良反应,与 Oostveen AM 等人研究结果相符[20]。

综上所述,清热散结片联合阿维 A 胶囊治疗难治性银屑病的疗效显著,能够明显缓解患者机体的炎性反应,值得临床推广应用。

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