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复方金银花煎液湿热敷与夫西地酸乳膏联合治疗靶向药物所致皮疹的临床疗效 *

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摘要 目的:分析复方金银花煎液湿热敷与夫西地酸乳膏联合治疗靶向药物所致皮疹的临床疗效。**方法:**选择 2014 年 8 月~2016 年 8 月我院收治的靶向药物所致皮疹患者 80 例,参照抽签法分作对照组与观察组,每组各 40 例。对照组患者采用夫西地酸乳膏治疗,观察组患者采用复方金银花煎液湿热敷与夫西地酸乳膏治疗,比较两组治疗前后症候积分、生活质量评分的变化、临床疗效和不良反应的发生情况。**结果:**治疗后,观察组症候积分(6.87± 1.25)分显著低于对照组(10.29± 2.74)分(P<0.05),生活质量评分(3.15± 0.57)亦明显低于对照组(6.42± 1.20)分(P<0.05)。观察组临床有效率(95.00%)显著高于对照组(77.50%),差异有统计学意义(P<0.05);两组不良反应的发生率比较差异均无统计学意义(P>0.05)。**结论:**复方金银花湿热敷与夫西地酸乳膏联合治疗靶向药物所致皮疹的临床疗效确切,可有效缓解患者临床症状,提高生活质量。

关键词:靶向治疗;皮疹;复方金银花煎液湿热敷;夫西地酸乳膏;临床疗效

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Clinical Efficacy of Compound Honeysuckle Decoction Hot and Humid Joint Fusidic Acid Cream in Treatment of Targeted Drugs-induced Rash*

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ABSTRACT Objective: To analyze the clinical efficacy of compound honeysuckle decoction hot and humid joint fusidic acid cream in the treatment of targeted drugs-induced rash. **Methods:** 80 cases of patients with targeted drugs-induced rash admitted in our hospitalfrom August 2014 to August 2016 were selected and divided into two groups with 40 cases in each group according to the drawing method. The control group was treated by fusidic acid cream, while the observation group was treated by compound honeysuckle decoction hot and humid joint fusidic acid cream, the changes of symptom score, quality of life after treatment, clinical efficacy and incidence of adverse reactions were compared between two groups. **Results:** After treatment, the symptoms score of observation group ((6.87± 1.25) points) was lower than that of the control group ((10.29± 2.74) points)(P<0.05), the quality of life score ((3.15± 0.57) points) of observation group was lower than that of the control group ((6.42± 1.20) points)(P<0.05). The effective rate of observation group(95.00%) was higher than that of the control group(77.50%)(P<0.05), no statistical difference was found in the incidence of adverse reactions was observed between two groups (P>0.05). **Conclusion:** Compound honeysuckle decoction hot and humid joint fusidic acid cream was effective in the treatment of targeted drugs-induced rash, it could effectively relieve the clinical symptoms, improve the quality of life.

Key words: Targeted therapy; Rash; Compound honeysuckle decoction hot and humid; Fusidic acid cream; Clinical efficacy

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前言

目前，靶向治疗已逐渐成为肿瘤治疗的常见有效治疗方式,其中分子靶向治疗是将特定的生物标记物选作靶点,使分子靶向药物可直接于靶点处发挥作用,从而达到杀灭肿瘤细胞的效果,其针对性相对较强,可显著提高患者的 5 年生存率[1,2]。但靶向药物却可引起系列毒副反应，以皮肤毒性反应最为常见,可造成不同程度的瘙痒、刺痛等症状,影响患者的生活质量,造成其耐受性降低,甚者停止用药,降低临床效果[3,4]。靶向药物所致的皮疹尚无特性临床治疗方式，主要以患处清洁、消除炎症等为主[5,6]。本研究在夫西地酸乳膏治疗基础上加以复方金银花煎液湿热敷治疗靶向药物所致的皮疹,取得了比较确切的疗效,现将结果报道如下。

1 资料与方法

1.1 一般资料

选择 2014 年 8 月~2016 年 8 月于我院行靶向药物所致皮疹患者 80 例,本研究家属及患者均签署知情同意书,且得到医

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院伦理委员会的许可。对照组有 29 例男性,有 11 例女性;年龄 40~75 岁, 平均 (54.62± 2.17) 岁; 靶向药物服用至起病时间 1~14 天,评分(7.24± 1.13)天;皮疹分级:有 7 例Ⅰ级,有 20 例Ⅱ级,有 13 例Ⅲ级。观察组有 26 例男性,有 14 例女性;年龄 42~73 岁, 平均 (53.08± 2.62) 岁; 靶向药物服用至起病时间 1~14 天,评分(6.11± 1.42)天;皮疹分级:有 5 例Ⅰ级,有 20 例Ⅱ级,有 15 例Ⅲ级。两组患者的一般临床特征比较差异无统计学意义(P>0.05),具有比较性。

1.2 纳入与排除标准

纳入标准[7]: 经过细胞学等检查明确为非小细胞肺癌;TNM 分期在Ⅲa 至Ⅳ期;均于吉非替尼口服 14 天内产生躯干、四肢的痤疮样皮疹;无心肝肾等主要器官严重病变;皮疹分级在Ⅰ~Ⅲ级(参照 MASCC 分级系统[8],Ⅰ级:脓疱及丘疹低于体表面积的 10%,可伴敏感或者瘙痒感;Ⅱ级:脓疱和丘疹为体表面积 10%~30%,伴压痛及瘙痒,可对日常生活造成影响;Ⅲ级:脓疱及丘疹超过体表面积的 30%,伴压痛及瘙痒,已对日常生活构成明显影响,且存在继发感染的危险)。排除标准:合并其他肿瘤;内分泌系统或者血液系统异常;非小细胞肺癌复发;既往伴皮疹史。

1.3 治疗方法

两组均于皮疹出现后开始用药,对照组采用夫西地酸乳膏治疗,常规消毒皮肤后,予以夫西地酸乳膏涂抹于患处,以皮疹全部覆盖,厚度 2 mm 为度。Ⅰ级每日用药 2 次,Ⅱ级 3 次,Ⅲ级 4 次。观察组复方金银花煎液湿热敷与夫西地酸乳膏治疗,将 30 g 金银花、30g 苦参加 3000 mL 清水并浸泡 20 min, 大火煮沸 5 min 后取文火煎煮 10 min,倒出药液并放至湿热(40℃),取棉质毛巾折叠 4 层左右,用药液浸湿,并轻拧毛巾以含药液但不滴水为度, 贴敷于患处,3 min 后加药液或者更换 1 次,以确保药液的有效温度, 每次湿热敷需持续 20 min, 每天实施 2~3 次。并于 5 min 后于患处均匀涂抹夫西地酸乳膏,方法同对照组。两组均持续治疗 30 天,期间密切关注患处情况,于治疗结束时评估临床疗效,并记录不良反应的发生情况。

1.4 观察指标

评估患者治疗前及治疗结束时中医症候评分[9]:皮损累及部位数 1 个部位(2 分),2 个(4 分),3 个及以上(6 分);皮损面积小于 1 个自身手掌面积(2 分)、1~2 个之间(4 分)、3 个及以上(6 分);皮疹颜色较暗、局部伴轻微红肿(2 分),颜色发红、局部显著红肿(4 分)、红肿范围比较广泛且呈浸润性,颜色鲜红(6 分);仅伴小粉刺(2 分),可见粉刺和丘疹(4 分),可见粉刺、丘疹及脓疱(6 分);偶尔可见疼痛及瘙痒,不影响日常生活(2 分),疼痛及瘙痒呈阵法性,对日常生活可有影响(4 分),疼痛及瘙痒比较频繁,对日常生活造成严重影响(6 分);舌红,舌苔呈薄黄(2 分),舌鲜红,舌苔呈薄黄或者腻(4 分),舌鲜红,舌苔呈厚腻(6 分);脉象数(2 分),脉象滑(4 分),脉象细涩(6 分)。生活质量评估[10]:包含社交娱乐、日常活动、家庭、心理、生理、治疗 6 个方面,0 分表示无影响,1 分表示轻度,2 分表示中度,3 分表示重度,生活质量越高分数则越低。临床疗效评估[11]:治愈:治疗后皮疹全部消退,瘙痒、疼痛等症状消失,症候评分减少在 90%以上;显效:皮损消退在 70%以上,症状显著缓解,症候积分减少超过 50%;好转:皮损消退低于70%,症状有所减轻,症候评分减少在 10%~20%;无效:皮损消退不明显,症状无改善或者加剧,症候评分无变化或者加重。治愈、显效及有效均视作有效。

1.5 统计学分析

选择 SPSS18.0 行数据统计, 计量资料用均数± 标准差($\bar{x}$± s)表示,用 t 检验比较,计数资料用[(n)%]表示,用 x^2 检验比较,以 P<0.05 为差异有统计学意义。

2 结果

2.1 两组皮疹患者治疗前后症候积分的比较

治疗前,两组症候积分比较差异无统计学意义(P>0.05);治疗后,两组症候积分均较治疗前降低,且观察组显著低于对照组,两组比较差异有统计学意义(P<0.05),见表 1。

表 1 两组皮疹患者治疗前后症候积分的比较($\bar{x}$± s)

Table 1 Comparison of the symptoms score between two groups of patients before and after treatment

Groups		Symptom score (points)
Control group(n=40)	Before treatment	22.79± 5.41
	After treatment	10.29± 2.74[a]
Observation group (n=40)	Before treatment	23.85± 6.20
	After treatment	6.87± 1.25[ab]

Note: Compared with before treatment, [a]P<0.05; Compared with control group, [b]P<0.05.

2.2 两组皮疹患者治疗前后生活质量评分的比较

治疗前, 两组生活质量评分比较差异无统计学意义(P>0.05);治疗后,两组生活质量评分均较治疗前降低,且观察组明显低于对照组,两组比较差异有统计学意义(P<0.05),见表 2。

表 2 两组皮疹患者治疗前后生活质量评分的比较($\bar{x}$± s)

Table 2 Comparison of the quality of life score between two groups before and after treatment

Groups		Quality of life score (points)
Control group(n=40)	Before treatment	15. 31± 3.98
	After treatment	6.42± 1.20[a]
Observation group (n=40)	Before treatment	16.74± 4.12
	After treatment	3.15± 0.57[ab]

Note: Compared with before treatment, [a]P<0.05; Compared with control group, [b]P<0.05.

2.3 两组皮疹患者临床疗效的比较

观察组临床总有效率为 95%,显著高于对照组,两组比较差异有统计学意义(P<0.05),见表 3。

2.4 两组皮疹患者不良反应发生情况的比较

治疗期间,两组均未见明显不良反应,对照组有 2 例瘙痒加重,有 1 例红斑加重,两组不良反应的发生情况比较差异无统计学意义(P>0.05)。

表 3 两组皮疹患者临床疗效的比较[例(%)]

Table 3 Comparison of the clinical curative effect between two groups of patients

Groups	Cure	Markedly	Better	Invalid	Effective rate
Control group(n=40)	1(25.00)	17(42.50)	13(32.50)	9(22.50)	31(77.50)
Observation group(n=40)	5(12.50)	27(67.50)	6(15.00)	2(5.00)	38(95.00)[a]

Note: Compared with the control group, [a]P<0.05.

3 讨论

肺癌是一种发病率最高的肺部原发性的恶性肿瘤,其中非小细胞肺癌约为肺癌的 80%,肺癌早期缺乏特异性症状,容易被自身所忽略,以至于约有 80%的肺癌患者确诊时已经进展为晚期,遗失了最佳的手术救治时间[12,13]。虽然常规抗细胞增殖药物能够导致肿瘤细胞凋亡,但残留的肿瘤细胞仍可通过周围的新生血管继续生长,其次异常的肿瘤血管能够阻碍药物进入肿瘤组织内,使其临床效果受到限制[14,15]。近年来,分子靶向药物成为非小细胞肺癌治疗的新型途径,吉非替尼是临床常用的靶向治疗药物, 可促使异常酪氨酸激酶的信号传导受到阻断,进而抑制肿瘤的生长及转移,促进肿瘤细胞走向凋亡,最终达到抗肿瘤目的[16,17]。但吉非替尼治疗期间能够引起皮肤反应,导致皮肤瘙痒、疼痛等,增加患者痛苦[18,19]。

夫西地酸乳膏是一种抗菌素,对葡萄球均等革兰阳性菌的敏感性极高,能够导致细菌蛋白质的合成受到抑制,发挥抗菌作用,其可透过深层皮肤,作用于感染病灶,使组织细胞的水肿及渗出等反应得到消除,从而起到确切的消炎作用[20,21]。夫西地酸乳膏的几乎无耐药性,能够长时间使用,现已广泛运用于临床皮肤科中[22]。

中医学认为皮疹为风、热、湿邪等所侵,临床治疗应于肺热、毒热等相结合,以清肺热、凉血、解毒等为主。复方金银花煎液中以金银花为君药,其性寒,味甘,入心、肺、胃经,能够起到凉散风热、消肿止痛、清热解毒之功,能够抑制金黄色葡萄球菌、绿脓杆菌、肺炎双球菌等病原菌,利于局部新陈代谢及血液循环的改善, 诱导肉芽组织形成增生, 促进皮疹创面的愈合[23,24]。苦参性寒、苦,入肝肾、大肠、胃经,能够有效抵抗机体炎症反应,缓解皮肤瘙痒,且对多种细菌均可起到抑制作用。相关研究报道,机体皮下的血管比较丰富,通过湿热敷等局部用药能够使药效直接作用于经脉,到达津液,起到药物归经之功效,且可避免放化疗患者胃肠道反应的加重[25,26]。同时,湿热敷能够促进低浓度组织液流向高浓度药液中,利于皮肤末梢血管出现收缩,从而使皮损渗出减少,炎症消退,且其传导作用能够使局部皮损的灼热、潮红感减轻,并且能够导致末梢神经的产生的病理性冲动受到抑制,起到止痒的目的[27]。此外,湿热敷能够促进表皮角质层形成软化,增加其通透性,清除皮损组织的坏死物质,利于药物的吸收[28]。

本结果显示:联合复方金银花湿热敷治疗后患者症候积分低于夫西地酸乳膏者,说明通过复方金银花湿热敷能够有效改善患者的临床体征及症状,促进皮疹消退。同时,联合复方金银花湿热敷治疗后生活质量改善更明显,说明其能有效提高患者的生活质量,减轻其痛苦。且联合复方金银花湿热敷治疗后患者有效率显著高于夫西地酸乳膏者,说明二者联合治疗能够显著增加药效,提高临床效果。且两组用药期间均未见明显不良反应,未影响患者进一步治疗,安全性均较高。

综上所述,复方金银花湿热敷与夫西地酸乳膏联合治疗靶向药物所致皮疹的临床疗效确切, 可有效缓解患者临床症状,提高生活质量。

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