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自体吸疱表皮移植术结合搔刮术治疗白癜风的临床评价

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摘要 目的:观察和比较搔刮术结合负压吸疱术和传统负压吸疱术对白癜风复色的疗效。**方法:**将 90 例稳定期白癜风患者随机分成搔刮术结合负压吸疱术组(45 例)和传统负压吸疱术组(45 例),分别给予搔刮术结合负压吸疱术和传统负压吸疱术治疗。治疗后,比较两组的复色情况,是否留有白斑缝隙,并进行白癜风疗效评价。进一步分析皮损部位、性别、临床类型对搔刮术结合负压吸疱术和传统负压吸疱术临床疗效的影响。**结果:**治疗后,搔刮术结合负压吸疱术组和传统负压吸疱术组在整体疗效无显著性差异(*P>0.05*)。搔刮术结合负压吸疱术组术后获得成片复色比例显著高于传统负压吸疱术组(88.9% vs. 4.4%,*P<0.001*)。不同性别患者接受搔刮术结合负压吸疱术和传统负压吸疱术的疗效比较均无统计学差异(*P>0.05*)。表皮移植术结合搔抓术组和单一表皮移植术组中,皮损发生在颈部、面部相比于躯干部、四肢、手足部的疗效明显更佳,局限型和节段型相比于散发型、肢端型的疗效更佳。**结论:**自体吸疱表皮移植术结合搔刮术用于稳定期白癜风的复色效果相比于传统自体吸疱表皮移植术疗效更佳。

关键词:白癜风;负压表皮移植术;搔刮术

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Clinical Evaluation of Surgery Blister Grafting Combined with Curettage in the treatment of Vitiligo

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ABSTRACT Objective: To observe and evaluate the efficacy of autologous vitiligo surgery blister grafting combined with curettage and traditional autologous vitiligo surgery blister grafting in the repigmentation of vitiligo. **Methods:** Autologous vitiligo surgery blister grafting combined with curettage (including 45 patients) and traditional autologous vitiligo surgery blister grafting (including 45 patients) were applied to 90 cases of patients with stable vitiligo respectively. The efficacy was evaluated by the repigmentation and the presence of remnant white macules. Further analysis was used to evaluate the influence caused by lesional site, gender, clinical types of vitiligo patients. **Results:** There was no significant difference in the total curative effects between autologous vitiligo surgery blister grafting combined with curettage and traditional autologous vitiligo surgery blister grafting (*P>0.05*). The proportion of integral repigmentation after vitiligo surgery blister grafting combined with curettage was higher compared with that of traditional vitiligo surgery blister grafting (88.9% vs. 4.4%, *P<0.001*). In addition, there was no significant difference in the gender between autologous vitiligo surgery blister grafting combined with curettage and traditional autologous vitiligo surgery blister grafting (*P>0.05*). The curative effect of vitiligo patients located in neck and face was better than that in trunk, limb, hand and foot. The curative effects of localized vitiligo and segmental vitiligo were better than acrofacial vitiligo and generalised vitiligo. **Conclusion:** The efficacy of autologous vitiligo surgery blister grafting combined with curettage is better than traditional autologous vitiligo surgery blister grafting to stable vitiligo patients.

Key words: Vitiligo; Suction grafting; Curettage

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前言

白癜风是一种获得性黑素细胞缺失引起的色素性皮肤病,临床上以皮肤一处或多处出现大小不等、形状各异的白斑为典型特征[1]。白癜风改变患者外貌,加重身心负担,影响正常社交生活,因此临床治疗以复色为最终目标,改善肤色不均匀尤为重要[2]。

白癜风治疗方法因临床分型和分期不同各异,主要治疗方法有外用激素、钙调磷酸酶抑制剂、口服激素、光疗和表皮移植等[3]。对于稳定期白癜风患者而言,自体吸疱表皮移植术治疗效果佳。表皮移植白癜风利用负压吸疱原理,将自体正常部位的表皮层移植至白斑皮损区,以改善原皮损区黑色素细胞缺失的情况。一般采用多孔吸盘置于白癜风患者皮损处和供皮区(选择腹部皮肤),同时以 30～60 kPa 的负压吸引表皮,形成疱皮,

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使表皮与真皮分离。水疱发生后，去除白斑处水疱表皮，将供皮区的疱皮平铺于去除疱皮的白斑处，并加压包扎。2 周后移植表皮成活，即有色素生成，4 周后黑色素加深扩大，3～6 个月色素扩大达最大限度[4,5]。某些特殊部位如面部及关节等不平坦部位，吸盘很难吸住，加大了表皮移植术的难度[6]。

负压吸疱术受吸盘形状的限制有一个显著的缺点，每个吸盘 1-6 孔不等，使得表皮疱和疱之间有缝隙，使得复色后出现铺路石样不均匀复色(见图 1)。为了克服这个缺点，我科运用搔刮术结合负压吸疱术改善复色不均匀现象，现报道如下。

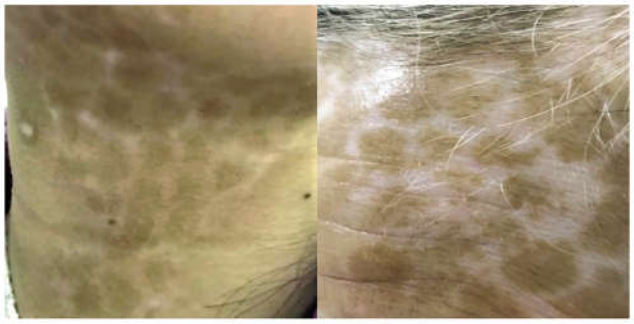


图 1 铺路石样不均匀复色

Fig.1 Typical photos of presence of remnant white macules.after suction grafting

1 材料与方法

1.1 临床资料

将 90 例患者随机分成搔刮术结合负压吸疱术组(45 例)和传统负压吸疱术组(45 例)。所有病人均处于白癜风稳定期，近一年无新发皮损。搔刮术结合负压吸疱术组：男 21 例，女 24 例；年龄 32.4± 1.88 岁；病程 8.0± 0.97 年；治疗部位及治疗区：面部 28 人、颈部 10 人、躯干部 3 人、四肢 2 人、手足部 2 人。传统负压吸疱术组：男 21 例，女 24 例；年龄 32.1± 1.59 岁；病程 9.7± 1.27 年；治疗部位及治疗区：面部 22 人、颈部 13 人、躯干部 3 人、四肢 3 人、手足部 4 人。两组患者性别、年龄、病程比较差异无统计学意义($P>0.05$)，具有可比性。

1.2 手术方法

自体负压吸疱表皮植皮术方法与常规方法相同[7]。先用表皮分离机同时对选定的健康供皮区和皮损区进行负压吸引，形成分离疱，根据吸疱情况，负压 30-60 kPa，吸引 60 分钟左右，无菌条件下依次疱皮剪下，弃去皮损区疱皮，供皮区疱皮移至皮损区，并予邦迪加压包扎。

1.2.1 搔刮术结合负压吸疱术处理受皮区 先负压吸疱使得表皮和真皮充分分离，无菌条件下用镊子进行搔刮。首先刮去组织分泌物和凝聚物，将疱和疱之间的缝隙部位进行均匀适度的搔刮，增加真皮层血供，使受皮区出现细小出血点。无菌纱布轻轻拭去渗血。将供皮区疱皮贴附在受皮区，并用邦迪覆盖贴紧。邦迪保留 2 周。1 月随访 1 次。在术后第 6 个月进行复色评估。

1.2.2 传统负压吸疱术处理受皮区 用 30-60 kPa 的负压表皮分离仪，受皮区吸取大小 1 cm 左右的疱皮，沿疱皮边缘剪下，将供皮区疱皮贴附在去除疱皮的受皮区，并用邦迪覆盖贴紧。邦迪保留 2 周。1 月随访 1 次。在术后第 6 个月进行复色评估。

1.3 疗效评价标准

根据经典植皮复色评价系统进行评估[8]，痊愈：移植皮片全部成活，白斑基本恢复正常；显效：被移植的白斑出现色素的面积 > 原白斑面积的 50%；有效：被移植的白斑出现色素并(或)逐渐向外扩大；无效：未出现色素或出现色素后又消失。有效率 = 显效 + 痊愈 / 总数；成片复色率 = 成片复色数 / 总数。

表 1 白癜风患者的基本信息

Table 1 The clinical characteristics of vitiligo patients

	Autologous vitiligo surgery blister grafting combined with curettage	Traditional autologous vitiligo surgery blister grafting	*P*
Gender(male/female)	21/24	21/24	>0.09
Age	32.36± 1.881	32.07± 1.594	0.2763
Duration	7.978± 0.9714	9.667± 1.272	0.0771
Lesion site			>0.09
Face	28	22	
Neck	10	13	
Trunk	3	3	
Limb	2	3	
Hand and foot	2	4	
Clinical types			>0.09
localized	8	10	
Segmental	20	18	
acrofacial	5	6	
generalised	12	11	

1.4 统计学分析

采用 SPSS20.0 软件进行统计分析,两组间计量资料的比较采用 t 检验,两组间计数资料的比较采用 x^2 检验,以 $P<0.05$ 表示差异具有统计学意义。

2 结果

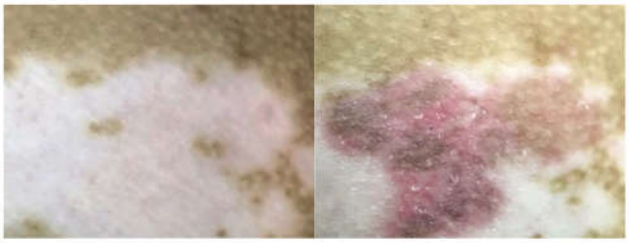
2.1 搔刮术结合负压吸疱术组和传统负压吸疱术组整体疗效及复色效果的比较

经统计学分析,搔刮术结合负压吸疱术组和传统负压吸疱术组在整体疗效无显著性差异($P>0.05$,表 2)。同时,我们对复色情况进行统计,结果显示搔刮术结合负压吸疱术组中 88.9%的患者获得成片复色效果 (图 2),而传统负压吸疱术组中仅 4.4%的患者获得成片复色效果(图 3),搔刮术结合负压吸疱术组术后获得成片复色比例显著高于传统负压吸疱术组 ($P<0.001$)。

表 2 搔刮术结合负压吸疱术组和传统负压吸疱术组疗效比较

Table 2 Comparison of the efficacy between autologous vitiligo surgery blister grafting combined with curettage and traditional autologous vitiligo surgery blister grafting

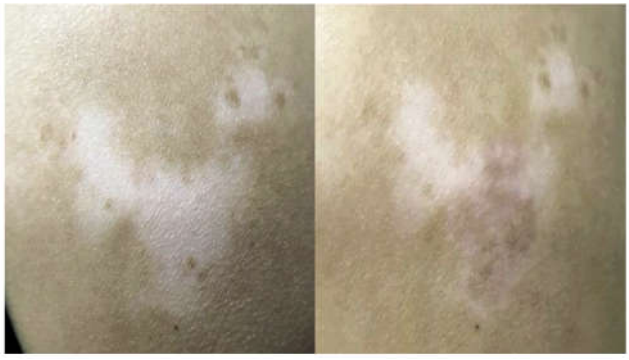
	Autologous vitiligo surgery blister grafting combined with curettage	Traditional autologous vitiligo surgery blister grafting	*P*
Total curative effects			
Healed completely well	32(71.1%)	34(75.6%)	0.2876
Marked effect	8(17.8%)	5(11.1%)	
Effect	5(11.1%)	6(13.3%)	
Without effect	0(0%)	0(0%)	
Repigmentation			
Complete repigmentation	40(88.9%)	2(4.4%)	<0.001
Remnant white macules	5(11.1%)	43(95.6%)	



Before treatment After treatment

图 2 搔刮术结合负压吸疱术后复色情况

Fig.2 Lesion after autologous vitiligo surgery blister grafting combined with curettage



Before treatment After treatment

图 3 传统负压吸疱术后复色情况

Fig.3 Lesion after traditional autologous vitiligo surgery blister grafting

2.2 搔刮术结合负压吸疱术和传统负压吸疱术临床疗效的影响因素分析

我们进一步分析了皮损部位、性别、临床类型对搔刮术结合负压吸疱术和传统负压吸疱术临床疗效的影响,结果显示:不同性别患者接受搔刮术结合负压吸疱术和传统负压吸疱术的疗效比较均无统计学差异($P>0.05$,表 3)。表皮移植术结合搔抓术组和单一表皮移植术组中,皮损发生在颈部、面部相比于躯干部、四肢、手足部的疗效明显更佳($P<0.05$,表 4)。局限型和节段型相比于散发型、肢端型的疗效更佳($P<0.05$,表 5)。

3 讨论

白癜风是一种表皮内黑素细胞缺失引起的色素脱失性皮肤病,临床上以大小不等的白斑为特征。白癜风的发病机制复

表 3 性别对疗效的影响

Table 3 The effect of gender(male/female) on the efficacy of therapy

Gender	Autologous vitiligo surgery blister grafting combined with curettage		Traditional autologous vitiligo surgery blister grafting	
	Cure rate	Complete repigmentation rate	Cure rate	Complete repigmentation rate
Male	90.5%	95.2%	95.2%	4.8%
Female	87.5%	83.3%	79.2%	4.2%

表 4 不同皮损部位疗效的比较

Table 4 Comparison of the efficacy between different lesion sites of repigmentation

Lesion site	Autologous vitiligo surgery blister grafting combined with curettage		Traditional autologous vitiligo surgery blister grafting	
	Cure rate	Complete repigmentation rate	Cure rate	Complete repigmentation rate
Face	96.4%	92.9%	95.5%	4.5%
Neck	90.0%	90.0%	100.0%	7.7%
Trunk	66.7%	66.7%	66.7%	0.0%
Limb	50.0%	50.0%	66.7%	0.0%
Hand and foot	50.0%	50.0%	50.0%	0.0%

表 5 白癜风临床分型对疗效的影响

Table 5 The effect of different clinical types of vitiligo on the efficacy of therapy

Clinical types	Autologous vitiligo surgery blister grafting combined with curettage		Traditional autologous vitiligo surgery blister grafting	
	Cure rate	Complete repigmentation rate	Cure rate	Complete Repigmentation rate
Localized	87.5%	100.0%	90.0%	10.0%
Segmental	100.0%	100.0%	100.0%	5.6%
acrofacial	60.0%	40.0%	83.3%	0.0%
generalised	83.3%	75.0%	72.8%	0.0%

杂,很多因素参与黑素细胞的破坏,比如自身免疫因素、遗传因素、炎症因素、氧化应激等等[9]。氧化还原状态异常、氧化应激增加及易感代谢异常是诱发免疫应答的重要因素,可导致黑素细胞退化和缺失[10]。白癜风根据临床分期分为活动期和稳定期。当病情处于活动期，临床治疗的主要目的是控制病情稳定,白斑不再新发。当病情进入稳定期后,临床治疗以复色为主。其中,复色是白癜风治疗的最终目标[11]。

自体负压吸疱表皮移植术是稳定期白癜风的重要治疗手段,效果可[5]。自体负压吸疱表皮移植术凭借无需麻醉、创伤小、方便快捷等优点,对小面积白癜风皮损疗效佳。自体负压吸疱表皮移植术取皮部位浅,位于表皮真皮分界处,不损伤真皮层,故愈后不留瘢痕;供皮区表皮疱底部含功能正常的表皮黑素细胞,在移植成功后,受皮区可正常复色[8]。本研究运用搔刮术结合自体负压吸疱表皮移植术,对负压吸引器多孔吸盘造成的疱皮间白斑缝隙进行搔刮,为供皮区疱皮黑素细胞缓慢爬行至缝隙部位提供存活条件,有效的改善了传统负压吸疱术引起的铺路石样复色的缺点。

研究表明白癜风色素脱失不仅由功能性黑素细胞缺失引起,功能异常的角质形成细胞也参与白癜风的发生发展[12]。供皮区疱皮内含相对正常的角质形成细胞以及黑素细胞,移植到受皮区,皮片成活后,在正常角质形成细胞的协同作用下,可产生黑色素,使受皮区恢复正常肤色[13]。此外,虽然色素脱失发生在表皮层,白癜风患者真皮层也参与发病的一环[14]。细胞与细胞间连接分子 E 粘附素的改变以及细胞内氧化还原水平持续性异常,应激导致白癜风非皮损区的黑素细胞中出现早衰表型[15]。真皮成纤维细胞表达和分泌角质细胞生长因子(keratinocyte growth factor, KGF)[16]。成纤维细胞和细胞外基质(extracellular matrix, ECM)在调节黑素细胞功能发挥重要作用。研究表明白癜风黑素细胞及色素正常区域的真皮成纤维细胞中氧化还原水平失衡,白癜风成纤维细胞产生的氧化应激产物与形态学和功能学变型有关[14]。同时,白癜风时,大量生物学特性类似成肌纤维细胞被发现[14]。成肌纤维细胞来源于不同前体细胞:除了来源于临近的成纤维细胞外,也可来源于其他常驻细胞,如平滑肌细胞、上皮细胞、内皮细胞、组织来源间充质干细胞、骨髓来源细胞[17]。线粒体功能损伤导致细胞内活性氧(reactive oxygen species, ROS)水平增高,真皮成纤维细胞内在缺陷,并且促进肌成纤维细胞分化。成纤维细胞线粒体复合物 I 异常产生高水平的 ROS,与平滑肌肌动蛋白 -α (alpha smooth muscle-actin, α-SMA)表达增多相关,最终导致向肌成纤维细胞内转移[18]。白癜风皮损中活性氧明显增加[15]。Wnt 通路抑制因子(Dickkopf1, DKK1)是黑素细胞增殖和色素产生的抑制因子[15]。调节黑素细胞稳态的细胞生长因子在包括白癜风的多种色素性疾病中极其重要 [19]。虽然很少有关于白癜风真皮改变的报道,绝大多数报道聚焦于表皮,但逐渐有研究表明真皮改变参与白癜风发病，上调的抗粘着 ECM 蛋白的固生蛋白和 DKK1 在真皮中表达[20]。

搔刮术结合自体负压吸疱表皮移植术,不仅有效的清除了负压引起的皮肤组织渗出物，避免异物影响黑素细胞存活;搔刮术通过刺激真皮层血流,使得受皮区提供更好的血供,有利于黑素细胞存活。此外,搔刮术破坏真皮层的异常的氧化还原水平,为移植的黑素细胞提供良好的生长环境。组织外伤(如搔刮等) 的修复，与结缔组织和炎症细胞释放的细胞因子相关[21,22],这些因子可加速黑素细胞代谢。血清中的细胞因子也可能是这种活化代谢的重要一环[23]。表皮外伤引起角质形成细胞产生碱性成纤维细胞生长因子，激活黑素细胞酪氨酸激酶受体,其后供皮区黑素细胞 mRNA 发生转录[24]。

黑素细胞能否存活与细胞代谢状态和酪氨酸酶活性相关[25,26]。酪氨酸酶是黑素细胞合成黑素小体的关键媒介,其功能异常参与白癜风自身免疫机制[27]。近期研究显示线粒体代谢异常可导致黑素细胞功能异常[28,20]。相比于未治疗的白癜风皮损,简单的搔刮可刺激白癜风皮损, 从而使酪氨酸酶 mRNA 从阴性转化为阳性,黑素细胞比例增加;同时,相比于单纯的表皮移植术,结合搔刮术可使黑素细胞酪氨酸酶 mRNA 轻度增加。移植后的供皮区黑素细胞的增殖需代谢物的刺激。因此,激活正常表皮基底层黑素细胞酪氨酸酶 mRNA 活性, 对顽固的白癜风皮损复色提供有利条件[21,29]。

本研究结果显示表皮移植术结合搔抓术和单一表皮移植术治疗的男性疗效均高于女性,但无显著性差异,提示性别对其疗效无明显影响。而皮损发生在颈部、面部的疗效相比于躯干部、四肢、手足部更佳,局限型和节段型疗效相比于散发型、肢端型更佳。国内外也有很多报道显示节段型白癜风易发生于颈部、头面部,且节段型白癜风病情容易控制,并且对自体移植术效果好[30]。

综上所述,自体吸疱表皮移植术结合搔刮术应用于白癜风的成片复色率高,可有效改善传统负压吸疱术的留有白斑缝隙的缺点,在治疗小面积白癜风白斑有效率高,使患者更好的复色,同时减少术后感染机会。

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