Photo- and laser therapy in pigment disorders
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PUNCH GRAFT TESTING IN VITILIGO; EFFECTS OF UVA, NB-UVB AND 632.8 NM HELIUM-NEON LASER ON THE OUTCOME


**ABSTRACT**

In a randomised controlled observer-blinded study including six patients with stable vitiligo the effects of UVA, NB-UVB and Helium-Neon laser irradiation on the outcome of punch-grafting were studied. In each of four 2x2 cm depigmented test-regions, four 1.5 mm pigmented punch grafts were placed. These test-regions were randomly allocated to the phototherapeutic modalities twice weekly versus no therapy at all during three months. In two patients the majority of punch grafts survived, whereas in the other four patients the majority of punch grafts depigmented. We concluded that stable vitiligo did not preclude failure of punch grafting. Intrinsic patient-related factors in the grafted area seem to determine outgrowth of pigment, while the phototherapeutic modalities have minor to no effect. The number of patients who showed pigment outgrowth was too small to compare the different modalities.

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INTRODUCTION

Vitiligo is an acquired disease characterised by progressive loss of melanocytes leading to the formation of white patches of the skin. It affects probably 1-2% of the world’s population, regardless of age, sex and skin colour [8]. The disease can alter a patient’s appearance dramatically, which often leads to social and psychological distress [6]. To date, non-segmental vitiligo cannot be cured, but with narrowband (NB) UVB phototherapy considerable repigmentation can be achieved [7]. In therapy-resistant non-progressive vitiligo, autologous punch grafting is widely used, as it is relatively inexpensive, easy to perform, and successful [1,9]. Post-operative irradiation (sunlight, UVA, NB-UVB) has been suggested to improve pigment outgrowth after punch grafting [4], but is unpractical and probably promotes photoageing and photocarcinogenesis. Recently, the red Helium-Neon (HeNe) laser (632.8 nm) was introduced as a safe potential inductor of repigmentation in vitiligo. The mechanism of action remains partly unclear, but as the HeNe laser is a low energy laser, thermal effects on the irradiated tissue are considered to be minute and effects are generally attributed to direct biostimulation of exposed cells [5,10]. Aim of this study was to evaluate pigment outgrowth of punch grafts after irradiation with UVA, NB-UVB and HeNe laser as compared to no phototherapy in patients with non-segmental vitiligo.

MATERIALS AND METHODS

The study protocol has been approved by the local medical ethical committee. This trial was conducted according to the Declaration of Helsinki Principles. A randomised controlled observer-blinded study was performed in six patients, older than 18 years, with non-segmental, stable vitiligo (VIDA score 0). Stability was defined as absence of progression during the last year. None of the patients had therapy for at least one year before inclusion. All patients were recruited from the outpatient clinic of the Netherlands Institute for Pigment Disorders at the Academic Medical Centre in Amsterdam. Written informed consent was obtained from all patients. In each patient four similar depigmented test-regions of approximately 2x2 cm were determined on the torso or proximal upper extremities. The test-regions were outlined on a transparent plastic sheet that was used to make a template from tin foil. In each of these depigmented test-regions four 1.5 mm pigmented punch grafts (with a surface area of 1.8 mm²) from the hip area were placed (Fig. 1a-b). The four test-regions were randomly allocated to receive either no phototherapy, UVA, NB-UVB, or HeNe laser twice weekly on non-consecutive days during three months, resulting in a total of 24 phototherapy sessions. All sessions were performed by the same physician. A UVA (BB-UVA; 320-400 nm) facial tanner (HB 171, Philips BV, Eindhoven, the Netherlands) was used at a power density of 8 mW/cm². The exposure time was increased from 4 minutes during the first phototherapy session to 8 minutes (second session) and 12
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minutes (third session). From the fourth until the last session the exposure remained 14.5 minutes. A 311 nm NB-UVB hand-held device was used (Waldmann TL 01, Villingen-Schwenningen, Germany) at a power density of 8 mW/cm². Treatment was started at 0.1 J/cm². This dose was increased by 0.1 J/cm² at each treatment if no side effects were reported. In accordance to previous studies, a red continuous wave HeNe laser with an average power of 1.0 mW was used for 30 seconds per punch graft, at an average distance of 10 cm. During each phototherapeutic treatment a tin foil template was used to prevent irradiation of the other three test-regions. Directly after the last phototherapeutic treatment (T₁), and at three and six months after the last treatment (T₂ and T₃) a blinded physician measured the largest (d₁) and its perpendicular diameter (d₂) of each punch graft in all treated areas. For each punch graft, the (re)pigmented surface area A was calculated by A = 0.25 π d₁d₂.

RESULTS AND DISCUSSION

At the start of the phototherapy (T₀) each patient had a total of 16 pigmented grafts (1.8 mm²) in four depigmented test regions. After 24 phototherapy sessions (T₁) we noticed that in two patients the majority of punch grafts survived (Fig. 1c), whereas in the other four patients the majority of punch grafts depigmented (Fig. 1d), irrespective of phototherapy. During follow-up no re-activation of vitiligo was found in any patient under study. In the two responding and four non responding patients, mean age was 32 and 48 years and mean disease duration was 16 and 23 years, respectively. One responding and one non responding patient had thyroid disease. The mean surface area per punch graft, for all patients, is shown in Fig. 2.

In the present study there was no apparent difference in pigment outgrowth between UVA, NB-UVB, HeNe laser and no phototherapy. The reason for the large number of depigmented grafts in stable vitiligo is unclear. We suggest that some patients with stable non-segmental vitiligo are characterised by sustained anti-melanocytic activity in the depigmented patches.

The main limitations of this study are (i) a small number of patients, (ii) a relatively short treatment period of three months, and (iii) a high number of depigmented grafts.

These data suggest that intrinsic patient-related factors in the grafted area seem to determine outgrowth of pigment, while the phototherapeutic modalities have minor to no effect. Secondly, the number of patients (two) who showed outgrowth of pigment was too small to compare the different modalities. Finally, stable vitiligo does not predict successful transplantation. A punch graft-test is probably essential to predict successful outcome of punch grafting in non-segmental vitiligo [2,3,9].
Fig. 1 On the left elbow of a patient two of the four 2x2 cm test-regions were drawn in the vitiligo lesion (a). In each of the four test-regions four 1.5 mm biopsies were punched out and pigmented minigrafts from the hip area were placed (b). Directly after 24 phototherapy sessions (T1); pigment outgrowth in all 16 minigrafts was seen in one patient (c), whereas in another patient almost all minigrafts were depigmented (d).
Fig. 2 Mean pigmented surface area per punch graft (mm$^2$) per treatment modality (UVA, NB-UVB, HeNe laser or no treatment) during the course of study; in the two patients of which the majority of punch grafts showed pigment outgrowth (a), and in the four patients of which the majority of punch grafts depigmented (b). At $T_0$ in all patients each of four test-regions consisted of four 1.8 mm$^2$ pigmented punch grafts.

$T_0$ - start of treatment
$T_1$ - directly after 24 phototherapeutic sessions
$T_2$ - three months after last phototherapeutic session
$T_3$ - six months after last phototherapeutic session
REFERENCES