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ORIGINAL ARTICLE

SUCCESSFUL TREATMENT OF VITILIGO WITH PUNCH GRAFT FOLLOWED BY OUTDOOR TOPICAL PSORALEN PLUS ULTRAVIOLET A RADIATION

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Background and Objective – **Punch grafting is a therapy for vitiligo but, to our knowledge, its combination with outdoor topical psoralen plus ultraviolet A radiation (PUVA) has not yet been studied. This study was designed to evaluate the efficacy of combination of punch graft and outdoor topical PUVA in recalcitrant vitiligo.**

Methods – **The study was performed in Razi Hospital, Tehran in 2000. After obtaining informed consent, 20 patients with stable and refractory vitiligo (4 segmental, 8 focal and 8 generalized) underwent treatment with punch grafting. After 3 months, outdoor topical PUVA with 8-methoxypsoralen was instituted and continued for a maximum of 4 months.**

Results – **After the 3 months of punch grafting, only nine patients experienced 33 – 66% repigmentation. Four months after starting topical outdoor PUVA, 13 patients experienced 90 – 100% and three patients 25 – 50% repigmentation. One focal and three generalized patients showed no response.**

Conclusion – **The combination of punch grafting and topical PUVA may be an effective treatment in stable and intractable vitiligo, especially the segmental and localized types.**

Keywords • punch grafting • topical PUVA • vitiligo

Introduction

Vitiligo, a common acquired disease, is manifested by circumscribed depigmented patches. Histologically there is an absence of cutaneous melanocytes.[1]

Vitiligo can be classified into several types. The localized type includes segmental and focal vitiligo. Vitiligo vulgaris, acrofacial and universal vitiligo are classified as the generalized type. Ten percent of cases are localized and 90% are generalized.[2]

Treatment for vitiligo includes the use of topical corticosteroids, calcipotriol, topical or systemic methoxypsoralen, and oral psoralen plus ultraviolet A radiation (PUVA), ultraviolet B radiation (UVB), phototherapy, pseudocatalase plus calcium plus UVB, vitamin supplementation, melagenina, systemic corticosteroids, other immunomodulators, and topical L-phenylalanine in combination with UVA (PAUVA).[1, 2] However, such treatments usually induce incomplete repigmentation and occasionally the outcome is poor.[1 – 3]

Vitiligo patients, resistant to medical treatment, in exposed areas represent a therapeutic problem to physicians and an aesthetic problem to patients, especially those with dark skin. Several surgical procedures for the treatment of intractable lesions have been reported to be effective, including thin Thiersch grafts,[2] suction-blistered epidermis,[2 – 5] minigrafting,[6 – 8] and injection of noncultured and various cultured cell-grafting techniques.[9, 10] All employ melanocytes from the patient's normal skin to cover depigmented patches.[11] Cutaneous cultured autologous melanocyte grafting has excellent results, but this technique is expensive and time consuming. To achieve favorable results, up to 8 months is necessary. The minigrafting technique is relatively simple and can be used in an outpatient clinic with simple instruments. However, repigmentation due to minigrafting is usually incomplete after 3 months to 4 years. [2, 3, 6–

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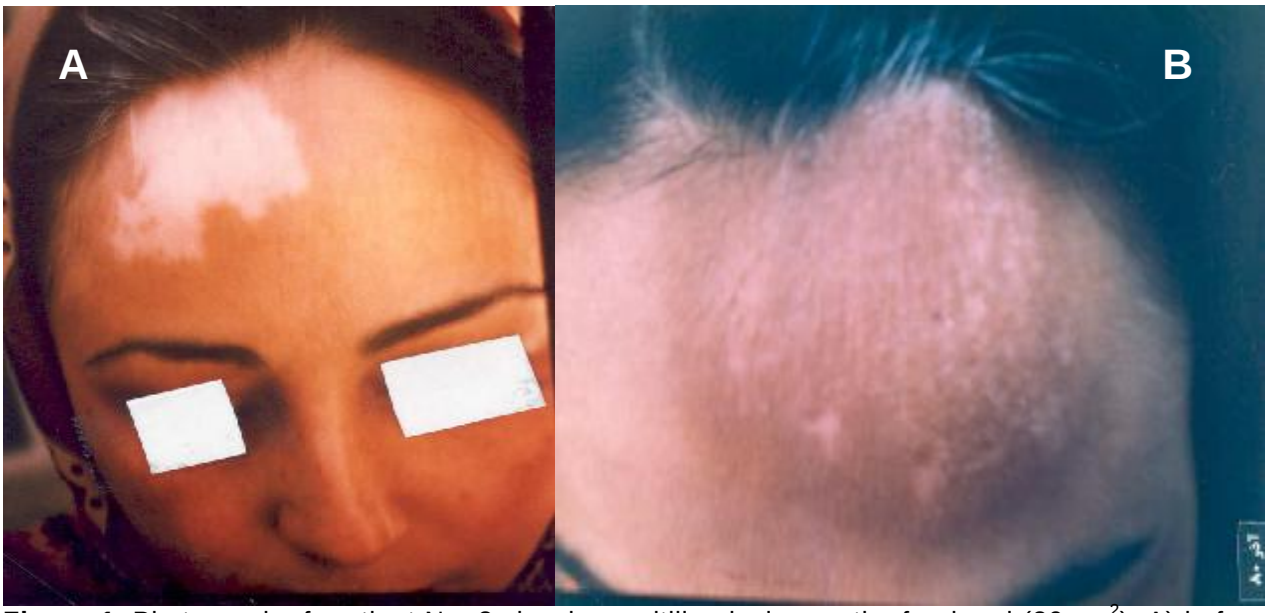

Figure 1. Photograph of patient No. 8 showing a vitiligo lesion on the forehead (20 cm^2): A) before grafting; and B) 7 months after grafting, showing 90% repigmentation.

[8]On the other hand, PUVA, either systemic or topical, increases the number of melanocytes and synthesis of melanin.[1, 4, 5] Topical outdoor PUVA is a popular, practical and efficacious therapeutic option for patients with limited vitiligo.[12] The mechanism of PUVA rests on the synergistic interaction of the two components (8-methoxypsoralen and UVA light) in the skin.[13] We conducted this study to evaluate the efficacy of combining punch grafting and topical outdoor PUVA in vitiligo patients.

Patients and Methods

Twenty Iranian patients (12 women and 8 men, in the age renge of 13 – 40 years) with stable vitiligo underwent minigrafting in Razi Hospital, Tehran in 2000. The disease was segmental in four, focal in eight and generalized in eight cases. All subjects were otherwise healthy. They had been resistant to systemic or topical methoxypsoralen and topical steroid therapies for at least 1 year. They showed neither spread of existing lesions nor development of new lesions during the previous 6 months. Patients under 12 years of age, pregnant and lactating women, and those with a history of photosensitivity or skin cancer were excluded from the study. After obtaining informed consent, one patch was grafted in each patient without previous minigrafting test.

The grafting site was prepared by infiltration of 1% lidocaine without epinephrine followed by perforation of recipient holes of 1.5 mm deep and 2.5 mm apart from each other. Minigrafts were harvested from the gluteal region for the trunk and limb regions, and the back of the ear for the face lesions; punches of 2 mm in size were placed within the recipient holes. Dressings were removed 2 weeks later and all subjects observed two sessions per month for 3 months. Repigmentation rate was scored visually. Graft rejection was determined as necrosis of the grafs in the recipient holes.

All subjects applied 8-methoxypsoralen (0.1% alcoholic solution) and received sunlight for three sessions per week, for a maximum of 4 months. The first exposure time was 15 seconds and was increased by 10 seconds per session until the appearance of a slight erythema. Treatment was continued until complete repigmentation occurred, or for 4 months. If no evidence of repigmentation was observed by this time, treatment was discontinued and repigmentation was scored. Data are presented as mean ± standard deviation.

Results

Three months after punch grafting, only nine (45%) patients experienced 33 – 66% repigmentation (partial repigmentation). The onset of repigmentation was between 28 and 45 days (35.3 ± 7.5). Further repigmentation stopped between 45 and 75 days (61.7 ± 9.0). Four months after the institution of topical outdoor PUVA, 13 patients experienced 90 – 100% repigmentation (complete

Table. Demographic and results of 20 patients with vitiligo treated with punch graft and topical PUVA.

No. of patient	Age/ sex	Size of treated lesion (cm^2)	Type (disease)	Area	Repig. onset after graft/the end of repig. after graft	Repig. after graft (%)	Repig. after PUVA (%)	Skin type	Rejected graft
1	16/F	75	Segmental	Trunk	45/60	50	90	4	8
2	20/M	9	Generalized	Face	45/60	33	99	3	—
3	16/F	6	Focal	Lt foot	35/60	33	100	2	—
4	17/M	4	Generalized	Face	—/—	—	99	3	—
5	25/F	8	Generalized	Rt hand	30/75	33	99	4	1
6	15/M	4	Focal	Face	—/—	—	99	2	—
7	23/M	6	Focal	Face	30/60	66	99	3	1
8	40/F	20	Segmental	Face	30/60	33	95	2	—
9	27/M	15	Focal	Trunk	28/60	66	90	3	2
10	21/F	8	Segmenta	Trunk	—/—	—	99	2	—
11	15/F	3	Focal	Rt shin	45/75	75	33	3	—
12	22/M	8	Segmenta	Face	30/60	66	99	4	—
13	13/F	6	Focal	Face	—/—	—	95	2	—
14	13/F	3	Focal	Trunk	—/—	—	—	3	—
15	27/F	8	Generalized	Lt wrist	—/—	—	—	4	—
16	25/F	9	Generalized	Lt wrist	—/—	—	—	3	—
17	14/F	8	Generalized	Lt hand	—/—	—	—	3	—
18	24/F	10	Generalized	Lt hand	—/—	—	50	3	2
19	17/M	2.25	Focal	Face	—/—	—	50	2	—
20	19/M	7	Generalized	Face	—/—	—	25	2	—

Lt = Left; Rt = right; Repig. = repigmentation.

response) and three patients 25–50% repigmentation (partial). Four patients showed no response. The mean onset of repigmentation was at 25.6 sessions (SD, 5.9 sessions). The results are summarized in the Table.

Nine patients who responded to punch grafting (33–66% repigmentation) showed complete repigmentation after PUVA. Punch grafting alone was unsuccessful in four of the patients who responded completely and in the three patients who responded partially (25–50%) to the combination of punch grafting and PUVA. Three (75%) responders had truncal, seven (70%) facial and three (50%) limb lesions. All subjects of segmental type, six (25%) subjects of localized type and three (38%) subjects of generalized type experienced 90–100% repigmentation (Figures 1 and 2).

The Kobner phenomenon was observed in three patients (2 patients with varying shape and size of recipient facial area and 1 in donor site). Cobblestoning was observed in 11 patients, but spontaneously resolved between 7 and 18 months later. Graft rejection was observed in only 14 (3%) out of 445 grafts.

Discussion

Falabella pioneered the use of small autotransplant for the treatment of four patients with segmental vitiligo in 1983.[7, 8] In 1988, he treated 22 patients with localized vitiligo after three to five minigraft tests by this method. Thirteen patients obtained 90 – 100% repigmentation.[8]

Westerhof et al also observed satisfactory results using minigrafting in stable leukoderma.[6]

Boersma et al evaluated autologous minigrafting followed by UVA (10 J/cm^2) twice a week in stable vitiligo vulgaris and found it effective in a selected group of patients. The results of 19 patients were analyzed, showing 80 to 99% repigmentation in 14 lesions, 50 to 80% repigmentation in 10 lesions, and zero to 50% repigmentation in 12 lesions.[2]

Although minigrafting can be an effective treatment in vitiligo, failure to achieve complete repigmentation in a high percentage of patients remains a major drawback.[2, 3, 6 – 8]

The potential of PUVA to increase the number of melanocytes prompted us to use autologous minigrafting followed by topical outdoor PUVA in 20 patients with stable vitiligo (segmental, vulgaris, and focal). We did not perform a minigraft test.

In the first phase of our study, only nine patients showed partial repigmentation (33 – 66%) by minigrafting. Repigmentation progressed mainly during the first 2 months and remained stable afterward, despite the sunny climate.

The addition of topical PUVA increased the rate of repigmentation significantly. Repigmentation reached 90 – 100% in 13 patients (including those patients who were responding to minigrafting). Three nonresponders to minigrafting showed 25 – 50% repigmentation with the addition

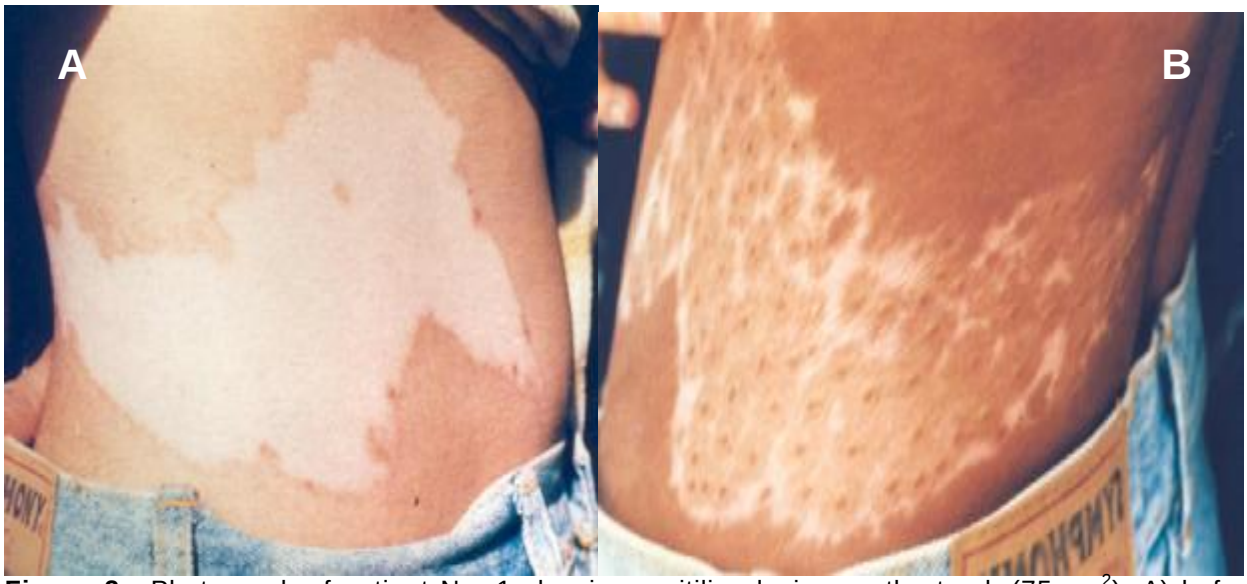

Figure 2. Photograph of patient No. 1 showing a vitiligo lesion on the trunk (75 cm^2): A) before grafting; and B) 7 months after grafting, showing 90% repigmentation.

of PUVA, while four patients (3 generalized, and 1 localized) showed no repigmentation despite the addition of PUVA.

Fitzpatrick skin type IV patients responded better than other types. Also, the response rate was higher on the trunk, followed by the face and extremities. Segmental vitiligo responded better than focal type. The least responsive group was the generalized type. Complete response to PUVA in four nonresponders to minigrafting and partial response in three nonresponders was an interesting finding in our study. This can be explained by the effect of methoxypsoralen plus UVA on the donor's melanocytes.

Kobner phenomenon was seen in two patients after minigrafting at recipient sites and in another one at the donor site. Cobblestoning was seen in 55% of patients. Repigmentation was nearly uniform.

After 1 year of follow-up, no hyperpigmentation was seen and only cosmetically acceptable mild cobblestoning was noted in 7 patients and resolved in others. Other possible side effects such as infection, hypertrophic scarring, keloids, persistent pigmentary changes and necrosis of the grafts were not seen. The combination of punch grafting and topical PUVA was an effective treatment in a small group of stable and intractable vitiligo, especially segmental and localized types.

We suggest further studies to evaluate whether earlier institution of PUVA after minigrafting leads to an earlier satisfactory response. Also, we suggest comparing this method with other techniques such as Thiersch grafting and suctioning blister epidermis in combination with PUVA or narrow-band UVB phototherapy in further studies.

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