Original Article

Outcome of Minigrafting In Stable Vitiligo: An Insight from Libya

Fauzia Musbah

Department of Dermatology, Faculty of Medicine, University of Tripoli, Tripoli, Libya.

Corresponding e-mail: fauziamusbah@yahoo.com

ABSTRACT

Background and aims. Autologous with punch minigrafting has been suggested as an alternative surgical method for treating stable vitiligo in refractory patients to induce repigmentation. The current study was conducted to evaluate the long-term results of surgical punch minigrafting in patients with resistant vitiligo vulgaris, segmental and focal vitiligo. **Methods:** Case series prospective exploratory study design was performed in Tripoli central hospital (TCH) and private clinic among patient with confirmed vitiligo vulgaris, segmental and focal vitiligo, during the period from 2009 -2019. Data were presented as descriptive statistics using SPSS version 22. Chi-square test was used to test the significance of data with the level of 0.05 considered as significant level. **Results:** A total of 28 patients presented with vitiligo, of them 26 (92.9%) were females and 2 (7.1%) were males, with age ranging from 11-46 years old. The re-pigmentation of vitiligo was (53.6%) vulgaris, (28.6%) segmental, and (17.9%) focal vitiligo, with stable disease that did not have any new lesions at least 12 months with the disease ranging from one year (7.2%) and up to 30 years. The main instruments used with these cases were; skin punch size between 2mm (28.6%), 2.5mm (32.1%), and 4 to 6mm (10.7 %). The donor sites were selected to match the recipient sites either behind ear 39.3%, thighs 43%, while 3.6% were not previously affected by the disease. **Conclusion.** It has been suggested that mini grafting is a proper treatment option for treating patients with stable vitiligo, by using a small size punch, that is less than 2mm.

Keywords: Punch, Minigrafting, Vitiligo, Vulgaris.

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INTRODUCTION

Vitiligo is a result of disrupted epidermal melanization with an undecided etiology and incompletely understood pathogenesis. It has a profound psychological impact and greatly affects the quality of life [1]. Depending on the type, extent, and duration of vitiligo, conventional medical therapies such as topical and systemic corticosteroids, topical immunomodulators, and phototherapy are not always successful, and repigmentation is often incomplete [2].

Vitiliginous lesions occurring on sites such as lips, acral areas, nipples, and genitals are particularly resistant to medical treatment. This has led to the evolution of various surgical modalities to treat recalcitrant stable lesions. Behl et al. 1964 was the first to describe the surgical treatment of vitiligo in a large series of 107 Indian patients with thin Thiersch grafts [3].

The conventional surgical modalities for vitiligo punch grafting, suction blister grafting, and thin split thickness skin grafting were described by Falabella et al. in 1971, where they designated the suction blister technique for repigmentation of vitiligo [4]. Later, the miniature punch grafting technique was developed in

1978 [5]. Thereafter, in 1989, the use of in-vitro cultures of melanocyte-bearing epidermis for the treatment of vitiligo was implemented [6]. The use of epidermal suspensions obtained by trypsinization was first reported in 1992 by Gauthier and Surleve-Bazeille [7], and further improved by Olsson and Juhlin [8] via adding a melanocyte culture medium for additional growth. Kahn and Cohen [9] utilized the motorized dermatome to obtain ultrathin grafts for vitiligo, and later in 1996 Kahn et al. reported the use of a short-pulse carbon dioxide laser, to denude the recipient area [10]. Subsequently, the excimer laser and targeted phototherapy have been developed to treat vitiligo and mini grafting and NB-UVB [11]. Thus, surgical treatment of vitiligo has evolved over the centuries, even though the etiology and pathogenesis of vitiligo remain elusive.

In 1972, Norman Orentreich first reported auto graft repigmentation in humans. He treated a black woman with longstanding leukoderma, which followed a chemical burn many years back. He reported a maximum of 1 mm pigment spread from both the 1 and 2mm grafts [12]. In 1976, Labuono and Shatin made a similar observation after transplanting hair bulbs with hair punch grafting within the leucodermic scars of discoid lupus erythematosus (DLE) [13].

Before intending any surgical intervention in vitiligo, a proper assessment of the stability status is important [14]. In clinical situations, stability can be judged by simple indicators; history, lack of progression of old lesions and absence of development of any new lesion within a specified period (6 months to 2 years) and absence of a recent Koebner phenomenon. The grafts are placed directly from the donor (buttock/upper thigh) to the recipient areas and finally after 4 to 7 days the dressings have to be removed [15-17]. This speeds up the procedure and lessens the chance of infection. The adhesive gives excellent results to secure the graft and also has antimicrobial properties against staphylococci, pseudomonas, and E. coli [18].

Post-surgically the patients are exposed to PUVA [19, 20]/PUVASOL (Psoralen plus UVA from Sunlight) [17,21] or NB-UVB [11] or even kept as such in some studies [17]. Patients are followed up fortnightly for the initial two months and then monthly, until complete re-pigmentation is achieved, another important parameter was the post-graft appearance of re-pigmentation (AOR) time. It was found to be between 2 and 6 weeks, in different studies, with an overall average being approximately 21.6 days, as shown in one study [22]. The entire depigmented and grafted area is expected to be completely re-pigmented within 3-6 months, based on the area of grafting and the body part involved

In the donor site, after healing with secondary intention, minimal superficial scarring is expected and acceptable. Perigraft re-pigmentation is expected to start from around 3-4 weeks [11, 17]. Cobble stoning is regarded as the commonest of them all [11,21,23], It was observed that with time it got corrected in most of the cases. [21] In resistant cases corrective electro fulguration may be needed [24]. In this regard it is only apt to conclude that grafting should not be performed with punches more than 1.5mm in diameter. On face and lips, it should be even smaller (1.2mm or 1mm) [11, 25].

METHODS

Case series prospective exploratory study design was performed in Tripoli central hospital (TCH) and private clinic among patient with confirmed vitiligo vulgaris, segmental and focal vitiligo, during the period from 2009 -2019. Data were presented as descriptive statistics using SPSS version 22. Chi-square test was used to test the significance of data with the level of 0.05 considered as significant level.

RESULTS

A total of 28 patients presented with vitiligo, of them 26 (92.9%) were females and 2 (7.1%) were males, with age ranging from 11-46 years old. The re-pigmentation of vitiligo was (53.6%) vulgaris, (28.6%) segmental, and (17.9%) focal vitiligo, with stable disease that did not have any new lesions at least 12 months with the disease ranging from one year (7.2%) and up to 30 years (Table 1). All patients have contact with skin type III (14.3%) and type IV (82.1%) based on detailed information gathered on the base line and during the follow up. The main instruments used with these cases were; skin punch size between 2mm (28.6%), 2.5mm (32.1%), and 4 to 6mm (10.7 %).

Table 1: Repigmentation grade Crosstabulation

			Repigmentation grade				Total
			Excellent	Good	Poor	Regular	
diagnosis	focal	Count	2	2	0	1	5
		% within diagnosis	40.0%	40.0%	0.0%	20.0%	100.0%
	Segmental	Count	2	2	2	2	8
		% within diagnosis	25.0%	25.0%	25.0%	25.0%	100.0%
	Vitiligo	Count	0	1	0	0	1
		% within diagnosis	0.0%	100.0%	0.0%	0.0%	100.0%
	vulgaris	Count	6	5	1	2	14
		% within diagnosis	42.9%	35.7%	7.1%	14.3%	100.0%
Total		Count	10	10	3	5	28
		% within diagnosis	35.7%	35.7%	10.7%	17.9%	100.0%

The donor sites were selected to match the recipient sites either behind ear 39.3%, thighs 43%, while 3.6% were not previously affected by the disease. Regarding the recipient sites, there were 43.1% affected on the head and neck, 3.6% on the labia majora, 7.1% on the areola. Thereafter, surgical grafts were fixed in place in 92.9%, followed by the application of Ezelline solution 2% and sun exposure for 3 days per a week in most of the patients and 10.7% of patients used Elidel cream 1% twice daily. Uniform perigraft pigmentation was obtained during the 4 to 5 weeks, and the results were 92.9% recurrence of depigmentation in grafted skin in two patients (7.1%), and one patient (3.6%) was hypothyroid. The re-pigmentation grade was excellent in 35.7%, good in 35.7%, poor in 10.7% and regular in 17.9%. Excellent re-pigmentation grade was seen in 42% of vitiligo vulgaris, 40% of focal vitiligo, and 25% of segmental vitiligo ($P=0.823$). Long term follow-up shows that 2.1% of cases have got re-pigmentation, and 60.7 % presented with cobble stone complication. However, 82% of the patients didn't developed hypopigmentation or scar.

DISCUSSION

Vitiligo is a depigmented skin disease with world prevalence estimated between 0.5% and 2%, and can affect individuals from both genders and all types of skin [26]. It has a considerable effect on patient's quality of life, which can result in social concern, high level of anxiety, and even depression [27,28]. Many patients have resisted patches to conventional medicinal modalities and are often unsuccessful indicating the absence of melanocytes reservoir. Surgical treatment may be recommended as a therapeutic option for patients with stable disease and who did not respond well to the other types of treatment.

This study was conducted to explore vitiligo patients with punch minigrafting. The procedure involves the transfer of circular pieces or punches of skin tissue from the donor area into similar shaped pits that are made on the recipient skin. The size of these punches ranged from 2mm to 4mm and they are spaced 5-10mm apart on the recipient skin. Table 2 showing different punch sizes used in different studies.

Table 2. Punch Graft Size Used

Author (Reference)	year	Punch size diameter in mm
Das SS et al.[29]	1992	4
Jha, et al. [30]	1992	3 and 4

Post operation exposure to ultraviolet light was reported to augment the effect of punch grafting with better and rapid cosmetic result than monotherapy. We have used topical khellin (ezelline solution 2%), a plant derivative, a furanochromone as photosensitizer plus sun exposure as khellin, and it did not induce skin phototoxicity with UVA, rather re-pigmentation similar to psoralens [31,32]. Some patients have been successfully used topical immunomodulators alone or in combination with other therapeutic modalities [33], for instance; pimecrolimus cream (Elidel) 1% twice daily especially for patient's skin grafted for head and neck (Figure 1). Most of patients exhibited some degree of improvement which can dramatically improve quality of the life especially when the disease occurs in genitals [34]. Figure 2,4 showed that the patient was evaluated during the period of follow up after the procedure. The graft re-pigmentation is expected to start between 4-5 weeks which is similar to the reported studies shown in table 3.

Table 3. Appearance of re-pigmentation in different studies.

Athor(reference	year	Earliest appearance of repigmentation in days
Lahiri K, et al. [11]	2006	14
Lahiri K, et al[21].	1997	14
Malakar S, et al[17]	1999	16
Savant SS[35]	1992	30

The result of excellent repigmentation grade presented in figure 3-6 was 35.7%, and determined by the re-pigmentation scoring system in previous researches [36].

Figure 1: a-Punch grafting 2.5mm size on depigmented vitiligo patch at time of surgery. b- Cobble stone appearance with excellent repigmentation after 3 months

**Figure 2: a-Depigmented patches with vitiligo vulgaris female patient on back of the neck.
b- After minigrafting technique. C-Repigmentation after one year**

Figure 3: a- Thirty nine years old female patient with segmental vitiligo patch on the chin& anterior neck. b- The same patient with marked repigmentation after 5 years

Figure 4: a-Depigmented patches on right leg . b- Perigraft repigmentation

Figure 5: a- female patient with segmental vitiligo on forehead for 20years duration. b- Follow up picture after 4 years with excellent repigmentation.

Figure 6: a- Uniform perigraft repigmentation after 5 weeks on right labia majora & upper inner thigh. b- Repigmentation with residual flattening cobble stone

Recurrence and progression of the disease may be related to the associated autoimmune disease due to the clinical stability is important in patient's selection [37]. Studies have demonstrated that clinical stability does not always exclude the presence of an autoimmune disease process in patients with vitiligo. Roa et al. 2012 demonstrated an increase in the quantity of the TCD8⁺ and CD5RO⁺ lymphocytes in the vitiligo lesions and this was related to the lower stability and worse response to treatment melanocytes transplants [38].

Perigraft halo means the rim of depigmentation that remains at the outer edge of the vitiligo lesion in case of miniature punch grafting. It was reported in our study that peri graft halo was 50% which can be avoided or minimized by a proper surgical technique. The technique involves placing the grafts along the periphery first before going towards the center of the lesion to be treated.

The complication cobblestone appearance was decreased by using 2mm punch, and was decreased with the time, and in resistant cases we used dermivate cream under occlusion [39]. At the donor sites no infection or keloid have appeared mostly after healing with secondary intention minimal superficial scarring is expected and acceptable.

CONCLUSION

Most vitiligo patients obtained some degree of improvement in transplanted sites with autologous punch minigrafting followed by khelline solution, sun exposure, and immunomodulators in some patients. Further

prospective studies on larger number of patients should be done to determine the effect of stability of pigmentation achieved by this combination regimen. We suggest that mini grafting to be used as treatment for patients with stable vitiligo using a small size punch, that is less than 2mm.

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