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## Original Article

# Intralesional Injection of Follicular Hair Suspension with Excimer Laser versus Excimer Laser in Treatment of Vitiligo

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## ABSTRACT

### Article information

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**Background and aim:** Follicular hair suspension [FHS] is a novel therapeutic technique for the treatment of stable vitiligo. Rather than using the traditional procedures, hair follicle melanocytes are used as a source of melanocytes. The melanocytes of the hair follicle have a special characteristic that makes them a desirable source of donor cells. Therefore, we aimed in this study to detect the efficacy of intralesional follicular cell suspension with excimer light and excimer light only in the treatment of vitiligo.

**Patients and Methods:** Thirty patients of different age groups showing various clinical forms of stable vitiligo that has no progression of existing and/or no appearance of new lesions in the last two years were included in this comparative clinical trial.

**Results:** Patients who treated with [FHS] plus excimer light showed a higher percentage of improvement [ $59.43 \pm 26.55$ ] when compared with patients who treated with excimer light alone [ $36.03 \pm 27.87$ ] with p-value = 0.002. Also, the degree of improvement was better in patients who treated with the combination therapy when compared to the excimer alone with p-value = 0.009.

**Conclusion:** We found that follicular hair suspension is more effective, minimally invasive, and useful technique in the treatment of stable vitiligo.

**Keywords:** Stable vitiligo; Follicular hair suspension; Excimer light.



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## INTRODUCTION

Vitiligo is an autoimmune skin condition characterized by the loss of pigment cells in the epidermis, resulting in well-defined white patches that are frequently symmetrically distributed [1].

Vitiligo has been treated using a variety of medical and surgical techniques [2]. Surgery is one of the therapeutic options available for stable, resistant vitiligo that has not succeeded to respond to medication and light therapy [3].

Several surgical therapeutic options have been presented for management of stable vitiligo, but complete cure has not been achieved yet [4].

## THE AIM OF THE WORK

Hair follicle cell transplant is a promising method, that needs to be explored and implemented in the treatment of stable vitiligo. So far, the purpose of this study was to compare the efficacy of intralesional follicular cell suspension with excimer light and excimer light alone in the treatment of vitiligo in an attempt to achieve better management of such condition.

## PATIENTS AND METHODS

Thirty patients of different age groups showing various clinical forms of stable vitiligo were recruited from the outpatient clinic of Dermatology, Venereology and Andrology, Al-Azhar University, Assiut Governate during the period between October 2018 and December 2019. This clinical trial study was approved by the Committee of Local Institutional Ethics of Faculty of Medicine, Al-Azhar University. The number of meeting codes is three and the number of paper codes is eight. Informed written consent was obtained from adult participants, while in the case of children, we got the consent of their parents. The study is conducted in accordance with Helsinki standards as revised in 2013 [5].

Patients with a confirmed diagnosis of stable vitiligo that has no progression and no appearance of new lesions in the last two years [6], were included.

Patients less than 10 years, patients with extensive depigmented areas or who have a keloidal and bleeding tendency and patients

with ophthalmic diseases or who have a sensitivity to phototherapy were not allowed to participate in this study. The disease was diagnosed clinically and investigated using Wood's light to confirm the diagnosis.

A few hairs from the occipital region were clipped to about 2 mm in length. A hair follicle gripping forceps is then used to gently pull the hair follicle unit out. Depending on the density of the recipient area, 30 - 40 pigmented follicles are extracted. Then hair follicles were put in saline solution and then subjected to processing. Under complete sterile condition, the extracted hair follicles are washed three times in phosphate buffered saline [PBS] for about three times. The PBS contains antimycotics and antibiotics [streptomycin, penicillin, and amphotericin B] [2].

To prepare the single cell suspension, the hair follicles are treated at 37°C for 90 minutes with 0.25 percent trypsin and 0.05 percent ethylene diamine tetra acetic acid [EDTA]. After 15-20 min of incubation, the cells loosen from each other, then we transfer the hair follicles to another tube of EDTA and trypsin to stop the reaction and prevent the destruction of separated cells. After that, the pellet was centrifuged at 1000 rpm for 5 minutes to yield the final cell pellet. The resulting cell pellet is suspended in PBS once again [2].

The recipient area is sterilized using betadine and local anesthesia was injected into the vitiliginous area. 18g needle attached to syringe was used to perform the intralesional injection of the follicular cell suspension in the vitiliginous area. Finally, surgical dressing was put on, and the patients were observed for one hour after procedure.

Sessions of the excimer laser to the recipient area and to the other patch started after one week and were performed two to three times weekly.

**Statistical Analysis:** SPSS [Statistical Package for Social Sciences] version 23.0 program for windows was used for data processing. Continuous variables were presented as mean  $\pm$  standard deviation [SD] and had been compared using Student's t test. Categorical factors were presented as frequencies and percentages and had been compared using Chi-square test. P-values less than 0.05 were considered significant.

## RESULTS

This study was conducted on 30 patients with stable vitiligo, their ages ranged from 14-43 years with a mean of  $27.47 \pm 8.13$  years. The baseline characteristics of our studied population are shown in table [1].

There is a significant increase in the percentage of improvement in patients treated with FHS with excimer more than patients treated with excimer alone [P-value = 0.002], as shown in table [2].

As regards the degree of improvement, there is a significant difference between FHS with excimer versus excimer alone as the majority of patients treated with FHS with excimer had some degree of improvement more than patients treated with excimer alone [P-value = 0.009], as shown in table [3].

We did not find a significant relation between improvement and demographic data in patients treated by FHS with excimer, as shown in table [4].

**Table [1]:** Comparison between demographic data of vitiligo patients

Baseline characteristic		
Age (Years)	(Range) Mean $\pm$ SD	(14-43) $27.47 \pm 8.13$
Gender: n (%)	Male	8 (26.7)
	Female	22 (73.3)
Skin photo type: n (%)	III	10 (33.3)
	IV	15 (50)
	V	5 (16.7)
Family history: n (%)	Positive	6 (20)
	Negative	24 (80)
Duration of vitiligo (Years)	(Range) Mean $\pm$ SD	(1-18) $6.41 \pm 3.12$
Type of vitiligo: n (%)	Segmental	15 (50)
	Non-segmental	15 (50)
Laterality of vitiligo: n (%)	Unilateral	15 (50)
	Bilateral	15 (50)

**Table [2]:** Comparison between FHS with excimer versus excimer alone according to percentage of improvement

Percentage of improvement	FHS with excimer	Excimer alone	p-value
Mean $\pm$ SD	$59.43 \pm 26.55$	$36.03 \pm 27.87$	<b>0.002*</b>

**Table [3]:** Comparison between FHS with excimer versus excimer alone according to degree of improvement

Degree of improvement	FHS with excimer	Excimer alone	p-value
	n (%)		
Marked improvement	12 (40)	4 (13.3)	<b>0.009*</b>
Moderate improvement	7 (23.3)	6 (20)	
Mild improvement	8 (26.7)	6 (20)	
No change	3 (10)	14 (46.7)	

**Table [4]:** Relation between improvement and demographic data in patients treated by FHS with excimer

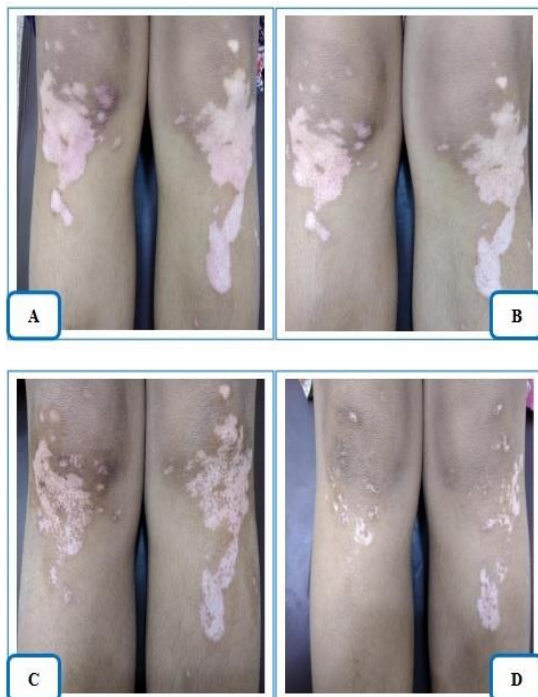
		FHS + Excimer	p-value
		Mean $\pm$ SD	
Gender: n (%)	Male	$59.38 \pm 33.96$	0.898
	Female	$59.82 \pm 24.26$	
Skin photo type: n (%)	III	$56.60 \pm 26.93$	0.613
	IV	$57.67 \pm 28.70$	
	V	$70.40 \pm 20.35$	
Family history: n (%)	Positive	$53.17 \pm 20.15$	0.528
	Negative	$61.00 \pm 28.07$	
Type of vitiligo: n (%)	Segmental	$61.27 \pm 21.24$	0.712
	Non-segmental	$57.60 \pm 31.65$	



**Figure [1]:** A 37 years old male patient presented with vitiligo patch on the left foot; upper patch treated by excimer light alone, and lower patch treated by FCS injection with excimer light (A: at baseline; B: after 1 month, C: after 2 months; D: after 3 months of treatment)



**Figure [2]:** A 32 years old female patient presented with vitiligo patch on the right leg; right patch treated by excimer light alone, and left patch treated by FCS injection with excimer light (A: at baseline; B: after 1 month, C: after 2 months; D: after 3 months of treatment)



**Figure [3]:** A 28 years old female patient presented with vitiligo patch on both legs; right patch treated by excimer light alone, and left patch treated by FCS injection with excimer light (A: at baseline; B: after 1 month, C: after 2 months; D: after 3 months of treatment)



**Figure [4]:** A 27 years old female patient presented with vitiligo patch on the right foot; right patch treated by excimer light alone, and left patch treated by FCS injection with excimer light (A: at baseline; B: after 1 month, C: after 2 months; D: after 3 months of treatment)

## DISCUSSION

Several therapeutic options for vitiligo are currently available; however, complete remission and patients' satisfaction have not yet been achieved [4].

Our study was conducted on 30 patients with stable vitiligo, with mean age of 27.47 years; in another study performed by **Mohanty et al.** [7], they reported older mean age of their participants [30.8 years]; however, other studies conducted by **Razmi et al.** [8] and **Vinay et al.** [9] reported a younger age of their studied patients [22.8 and 21.1 years respectively].

The variation of age can be explained by the work of **Jin et al.** [10] as they indicated that the age of onset is bimodal, with one-third of instances starting early and two-thirds starting later [mean 34.0 years]. Also, **Spritz** [11] reported that Vitiligo can develop at any age, regardless of skin type, gender, race, or geographic location, and is triggered by multiple inherited genes.

Epidemiological research has shown inconsistent results regarding the occurrence of this disease in both men and women. While some authors have found a higher proportion in males, others have reported a higher proportion in females, and others have found no difference in the proportion between both genders

In our study, the majority of patients were females, this comes in accordance with several researches [7-9, 12-14] as they reported a higher female to male ratio. Other authors found that there was no difference in both genders [15, 16]; however, **Anaba** [17] reported a higher proportion in male.

Indeed, the reason for the link between specific sex and the prevalence of autoimmune illnesses is yet unknown, however, **Patil et al.** [18] explained that, as women are more likely to attend clinics as they usually worry more about pigmentation changes of their skin and these changes usually affect their social life and this could be a possible reason for the female predominance in this study.

Authors who reported a higher proportion in males explained that trauma and koebnerization of lesions may have led to the affectation of more males than females [17].

In this present study, the family history of vitiligo was negative in 80% of patients. This comes in accordance with the study done by **Razmi et al.** [8] and **Singh et al.** [19].

In our study, the duration of lesion ranged between one to 18 years with mean of 6.41 years; this comes in accordance with the study done by **Vinay et al.** [9], as they reported a mean duration of 6.9 years. Also, in the study done by **Anaba** [17]; she reported that 89% of the studied population had a disease duration of more than one year, and the study done by **Razmi et al.** [8], they reported that the disease duration ranged between five and 13 years.

Excimer light can emit light with 308-nm wavelength. It has also been shown to be effective in inducing re-pigmentation of vitiligo lesions [20-22]. Our study showed superior re-pigmentation outcomes with FHS plus excimer vs excimer alone. In this study the mean of improvement in re-pigmentation in FHS with excimer was  $59.43 \pm 26.55$  versus  $36.03 \pm 27.87$  in the group treated with excimer alone.

In our study, 63% of patients treated with a combination of FHS plus excimer light showed marked to moderate improvement, however, only 10 % of patients showed this improvement in the excimer group. On the other hand, only 10% of patients showed no change in the group treated with both excimer and FHS versus 46.7 failure of improvement in the excimer group.

**Shah et al.** [23] treated 25 patients of stable vitiligo with follicular outer cell sheath suspension where follicular units were harvested by follicular unit excision [FUE] method. The mean of re-pigmentation observed was  $80.15\% \pm 22.9\%$  with excellent re-pigmentation [90–100%] in 60% of patients. Unfortunately, there is a lack of studies concerning with the combination between FHS plus excimer light in the treatment of vitiligo. However, in a trial of 40 stable vitiligo patients treated with ultra-thin split-thickness grafts followed by NB-UVB, > 90% re-pigmentation was achieved in 83 percent of the individuals, with satisfactory to excellent cosmetic effects in 90% of the recipient sites [24].

Our results also come in accordance with the study done by **Razmi et al.** [8], as they reported >75% re-pigmentation in 76.2% in epidermal cell suspension [ECS] + follicular cell suspension [FCS] vs 57.1% in ECS. Also,

another study conducted by **Donaparthi et al.** [25], reported >75% re-pigmentation in 43% of patients in FCS. **Singh et al.** [19] reported >75% re-pigmentation in 78% of patients who underwent FCS technique.

The improvement of re-pigmentation when FHS is combined with excimer could be attributed to special melanocyte characteristics and the presence of different stem cells [8]. The hair follicle contains three different types of stem cells, all of which appear to play a role in hair growth [26]. For every five keratinocytes in follicular melanin units, one melanocyte exists, however the ratio is less in the epidermis of the skin [1:36] [27]. Although, the melanocytes of hair bulb are larger, having more dendrites, Golgi and rough endoplasmic reticulum, and produce larger melanosomes than epidermal melanocytes [27]. Because the vitiligo patches' early re-pigmentation generally occurs around the hair follicles, so vitiligo patches lacking hair follicles, are often resistant to medical therapies, thus this reservoir of melanocytes and melanocyte stem cells is important in the treatment of vitiligo [28]. Also, FHS might also enhance the re-pigmentation through immunomodulatory effect of hair follicle mesenchymal stem cells [29].

In this study, we did not find a significant association between the age of patients, duration of vitiligo and improvement in patients treated by FHS with excimer. This comes in accordance with the study performed by **Vinay et al.** [9] as they declared that there was no significant difference in terms of gender, age, stability of lesion, total disease duration, site of lesion, between patients achieving re-pigmentation > 90% and not achieving re-pigmentation > 90%.

In this study, mostly all patients in both groups showed no adverse effect, however 23% in FHS with excimer had transient erythema versus 26.7% in the excimer group. Also, sporadic cases in FHS with excimer reported having a burning sensation and swelling besides the occurrence of erythema. **Razmi et al.** [8] reported the occurrence of hyperpigmentation at the skin donor site among their studied population, however none of their patients had scarring, koebnerization, or milia at the donor or recipient site.

To sum up our work, this study showed superior re-pigmentation outcomes with FHS plus excimer versus excimer alone, FHS is a

useful minimally invasive therapy for vitiligo resulting in good re-pigmentation with no visible residual scarring at the donor area.

Limitations of our study were small sample size and a short follow-up period. The observed results may be different in large sample size and a longer duration of follow-up, as the re-pigmentation after the surgery continues, another limitation was that the extraction of intact follicular units necessitates competence in order to get whole hair follicles while preventing hair follicle transection during extraction. In addition, excimer laser equipment is much more expensive than the NBUBV, the use of combination therapy using excimer laser, which can increase medical cost and burden to patients, has a limitation to be readily performed.

**Recommendation:** Further studies for comparison of the histopathological change in the immune cells at the site of the lesion with the level of disturbance in the peripheral blood are needed, also other studies are needed to clarify the clinical importance of our speculations.

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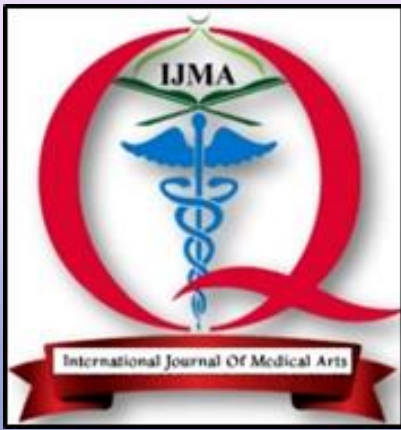
**Conflict of Interest:** All authors declare that they have no conflict of interest.

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