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IP Indian Journal of Clinical and Experimental Dermatology

Journal homepage: www.ijced.org/

Original Research Article

A study on autologous non-cultured melanocyte transfer in patients of stable vitiligo at a tertiary care centre

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ARTICLE INFO

Article history:
Received 05-04-2023
Accepted 02-05-2023
Available online 03-07-2023

Keywords:
Non-cultured melanocyte transfer
Vitiligo

ABSTRACT

Background: Vitiligo is an acquired pigmentary disorder caused due to a loss of functional melanocytes. Autologous non-cultured melanocyte transfer (NCMT) is a recent surgical modality for the treatment of stable vitiligo.
Objective: To evaluate the clinical outcome of NCMT in patients of stable vitiligo.
Materials and Methods: Autologous melanocyte transfer was performed on 41 patients of stable vitiligo. They were evaluated at 1, 4, 12, 18 and 24 weeks post-surgery for extent for repigmentation and complications.
Results: In this study, the male- female ratio was nearly equal, with 51% males and 48% females the mean duration of stability of vitiligo lesion was 3.39 years. By 24^{th} week of follow-up, 56.09% had excellent repigmentation (>90%), while 31.70% patients had good pigmentation (75-90%). No significant complications in donor area or recipient site were noted.
Conclusion: Autologous non-cultured melanocyte transfer is a quick, single day procedure, and can be performed on an out-patient basis. It requires lesser technicalities than other surgical procedures for treating vitiligo and can prove to be an effective treatment modality in achieving homogenous repigmentation with an excellent degree of patient satisfaction.

1. Introduction

The first description of vitiligo ages back to more than 3000 years ago.[1] It is a common disorder of depigmentation, characterised by chalky-white macules and patches of irregular shapes and sizes. It has a worldwide prevalence ranging from 0.5-1% and is a major cause of social discrimination worldwide and is often implicated in unemployment and difficulties in getting married.[2] The disease affects all races across the world, without a well demarcated gender predilection making it a very common depigmentary disorder. The estimated incidence is 0.5-1%; which is highest in India and Mexico, with peak incidences of upto 8.8% reported from India.[3] The prevalence of vitiligo in various studies among dermatology out-patients done across India ranges invariably from 0.25-4%, with highest incidences from Gujarat and Rajasthan.[4,5]

The etiopathogenesis of vitiligo is complicated, multifaceted, and essentially unknown. In 1979, Varma K in his study, came to a conclusion that vitiligo is a chronic smouldering inflammation, probably of the nature of autoimmune disorder.[6] The role of oxidative stress, autoimmune events, neuro-humoral factors, and auto-cytotoxic factors have all been the basis of several theories. The various factors of the disease have indeed contributed, and no one theory can be considered to be

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https://doi.org/10.18231/j.ijced.2023.011

mutually exclusive.[7] A comprehensive classification given by Vitiligo Global Issues Consensus Conference (VGICC) divides vitiligo into: segmental, non-segmental and mixed types.

Even in the present era, the management of vitiligo is particularly quite challenging in dermatology. Medical therapies are the primary treatment, but they depend upon the presence of a melanocyte reserve in the body and are therefore effective in only 60-70% of the patients. The surgical treatment for vitiligo first came into existence in the 1960s.[8] Over 3500 years ago, in ancient Egypt, the earliest attempts at skin grafting were conducted. More recently, one such management option which has gained immense popularity is the Non-cultured melanocyte/ keratinocyte transplantation (NCMT). It was first proposed in the year 1992, by the French researchers, Gauthier& Surleve-Bazeille.[9] It permits the treatment of the affected area many folds larger than the donor area. Further, it is a quick, single day procedure, and can be performed on an out patient basis with lesser requirement of technicalities. It can prove to be an effective treatment modality in achieving homogenous repigmentation with an excellent degree of patient satisfaction. With this background, the results of autologous non-cultured melanocyte transfer were further evaluated in patients of stable vitiligo who visited Dermatology OPD at a tertiary care centre in Central India.

2. Materials and Methods

This was a prospective, longitudinal study conducted on 41 patients of stable vitiligo who attended dermatology OPD.

2.1. Inclusion criteria

1. All patients with stable form of vitiligo, where stable vitiligo is defined by the following features
   (a) No new lesions since at least one year
   (b) No increment in the existing lesions since one year.
   (c) Absence of koebnerization.
2. Patients between age group 14-50 years.
3. Patients giving consent for the procedure.

2.2. Exclusion criteria

1. Immuno-compromised patients or patients with any existing active infection.
2. Patients who leave the study midway as a result of loss to follow-up.
3. Patients with keloidal tendencies.

2.3. Methodology

Pre-procedure informed consent was taken from each patient. Under aseptic conditions and after surgical cleaning, an ultra thin split-thickness skin graft was harvested using razor blade fitted into artery forceps from the antero-lateral aspect of thigh. It was washed in normal saline and transferred to a petri dish containing 5ml of 0.2% Trypsin-EDTA solution. This was then incubated at 37°C for 45 minutes. The mixture was again washed with normal saline and transferred to 8ml of melanocyte nourishment medium i.e. Dulbecko's Modified Eagle Medium (DMEM/F12) in a petri dish. After gently teasing the epidermis from the dermis using blunt forceps, epidermal contents were suspended in a test tube containing DMEM solution which was then centrifuged at 1500 rpm for 15 minutes to obtain the pellet. The recipient area was dermabraded upto the papillary dermis with a manual dermabrader (Figure 1). A thin film of epidermal suspension was spread uniformly over the dermabraded area and subsequently covered with collagen dressing for 7 days. The patient was followed- up at regular intervals to assess repigmentation. Topical medications were given to accelerate the rate of repigmentation.

The degree of repigmentation was evaluated on the basis of Visual Analogue System Score for extent of pigmentation and color match as: 0-25 % - Poor, 25-50% - Moderate, 50-75% -Marked, 75-90% - Good, >90% - Excellent.

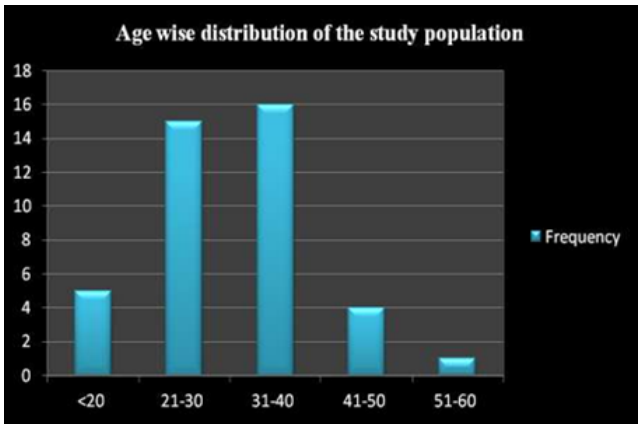
3. Results

The mean age of our study population was 31.27 ± 9.20 years (Graph 1). Maximum patients belonged in the age group 31-40 years. The male: female ratio was nearly equal with 51.22% males and 48.78% females. Most of the patients had non-segmental type of vitiligo (63.41%) with the remaining having segmental vitiligo. The mean duration of disease stability: 3.39 ± 1.97 years. Most of the patients had a stable vitiligo between duration of 2.1-4 years. The most common lesional site in this study was Lower limb 16(39.02%), followed by feet 10(24.39%), and least in the upper limb and hand with 6(14.63%) each (Graph 2). 15 (36.59%) had leukotrichia, and no patient had koebnerization. 7(17.07%) patients were associated with thyroid dysfunction, and 1(2.44%) had diabetes mellitus.

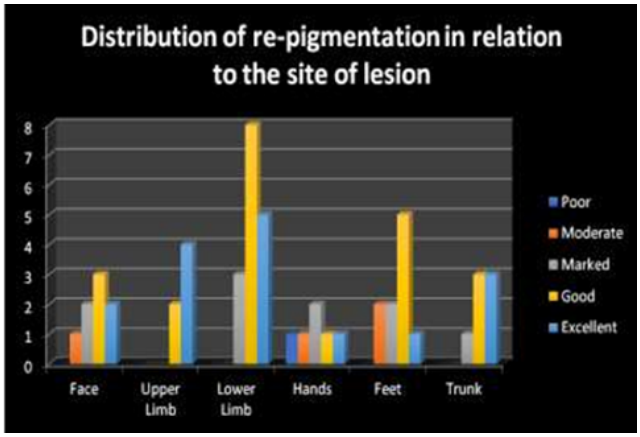
In the first week of follow-up, all the patients had poor repigmentation (Figure 2a,b). By the 4th week of follow-up, 21 (51.22%), had moderate grade of repigmentation, followed by 12 (29.27%) having poor repigmentation, and 8 (19.51%) had marked repigmentation.

By the 24th week of follow-up, 16(39.02%) patients showed good repigmentation i.e. 75-90%, while 14 (34.14%) showed an excellent repigmentation. Marked repigmentation was seen in 6 (14.63%) patients, followed by 4 (9.75%) with moderate repigmentation (Figures 3 and 4). One (2.43%) patient showed poor response.

Most of the patients, i.e. 13(81.25%) with lesions over lower limb had >75% repigmentation and a majority of the patients with a poor extent of repigmentation had



Graph 1: Age wise distribution of the study population



Graph 2: Distribution of repigmentation in relation to site of lesion

Table 1: Comparison of treatment outcome after 24 weeks

Study (n: sample size)	Poor (0-25%)	Fair (25-75%)	Good (>75%)
Present study (n: 41)	2.43%	24.38%	73.16%
Gill et al [10] (n: 50)	18%	20%	62%
Badad et al [11] (n: 50)	9.09%	13.64%	77.27%
Verma et al [12] (n: 25)	18%	20%	62%
Paul [13] (n: 58)	8%	8%	83%

Table 2: Comparison of complications in donor and recipient site

Study	Donor area	Recipient area
Present study	Scarring : 17.07%	Colour mismatch : 12.20%
	Dyspigmentation : 9.76%	Infection : 9.76%
	Infection : 4.88%	Scarring : 7.32%
Pandya et al [7]	Infection : 7.4%	Infection : 11.1%
	Koebner response : 1 case	
Badad et al [5]	Scarring : 9.09%	Erythema : 13.64%
	Depigmentation: 4.55%	
	Keloid formation : 4.55%	Infection : 9.09%

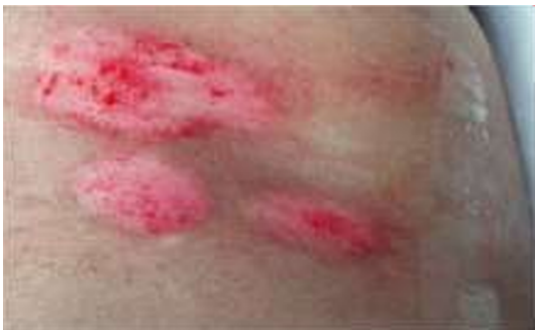


Fig. 1: Pin-point bleeding aftermanual dermabrasion

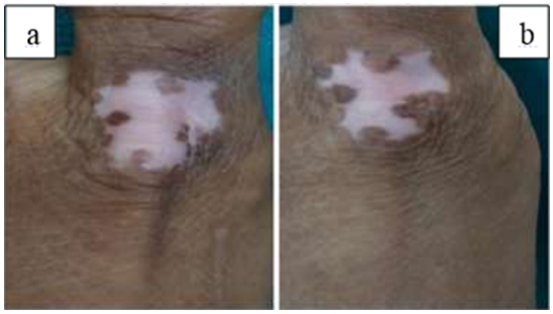


Fig. 2: a: Pre-treatment and **b:** at 4 weeks

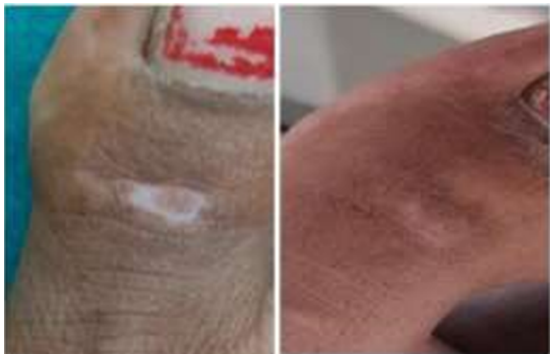


Fig. 3: Pre- and post- treatment (Patient 2)

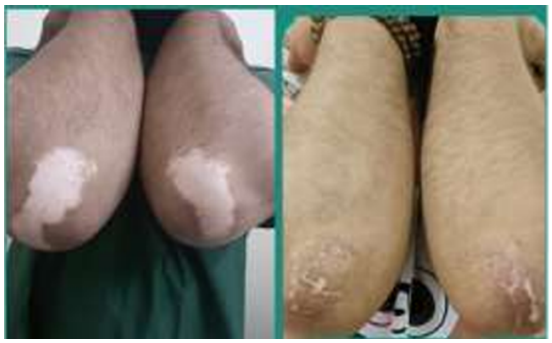


Fig. 4: Pre- and post- treatment (Patient)

lesions over hands and feet. The majority, 12 (46.15%) of the patients without leukotrichia had an excellent repigmentation. On analyzing the patients with leukotrichia, 6 (14.63%) had a good, followed by 3 (20.00%) had a moderate extent of repigmentation.

Majority of the patients did not develop any serious complications. Over the donor area, 7(17.07%) had scarring and 4(9.76%) had dyspigmentation (figure 5). Infection and keloid formation was seen in 2(4.88%) each, while cobble stoning was seen in 1(2.44%). Over the recipient area, 5(12.20%) developed colour mismatch, 4(9.76%) had an infection, 3(7.32%) had depigmentation, and 3(7.32%) had scarring.

4. Discussion

The present study was conducted at a Tertiary Care Centre. In this study, 41 cases of stable vitiligo were enrolled and Autologous non-cultured melanocyte transfer was performed after which they were followed up till 24 weeks to look for the extent of repigmentation. In our study, the mean age of study population was 31.27 ± 9.20 years. This finding was comparable to the findings of similar study conducted by Gill *et al* which had mean age of 29 ± 13.8.[10] In the present study, 63% patients had non-segmental vitiligo, while 36% had segmental. The proportion of segmental vitiligo was higher than the findings by Gill *et al* where segmental vitiligo constituted only 8% of the total.[10] The mean duration of the stability in our study was 3.39 ± 1.97 years. Majority, 16(39.02%) of the population had the duration of stability for 2-4 years, followed by 14(34.15%) had duration for <2 years. In the study done by Badad et al, 62% patients had stability of 6-10 years duration, while 12% had vitiligo of >11 years duration.[11]

In the present study, leukotrichia was present in 63.41% patients. On analysing the impact of leukotrichia in our study, it was concluded that patients without leukotrichia had better extent of repigmentation than those with leukotrichia. Hair follicle bulge contains stem cell reservoir for melanocytes. Leukotrichia is suggestive of exhausted melanocyte reservoir. It can be concluded that absence of leukotrichia is a good prognostic factor for repigmentation in vitiligo. Lontz *et al* in their study analysed that anatomical location of lesion is a major determinant of treatment outcome.[14] The extremities, elbows and knuckles showed a poor response. Similar observations were made by Pandya et al who reported poor response in patients with lesions over hands, feet and elbow.[15] The findings in our study were concordant with the above findings. Poor response over extensors can be subjected to a lack of melanocyte stem cell reservoir over these areas.

In their study, Gill *et al* observed good repigmentation (>70%) in 62% patients, fair repigmentation in 20% while 9 out of 50 patients (18%) showed poor response.[10] Badad *et al,* in their study on 22 patients, reported excellent repigmentation (>75%) in 17 (77.27%), with 3 (13.64%) showing good and 2 (9.09%) showing poor repigmentation.[11] The results of the present study are slightly lesser than the study done by Badad et al.[11] (Tables 1 and 2). A meta-analysis study done by Ju *et al* showed >90% pigmentation in 47.51% cases, while 63.42% cases showed >75% re-pigmentation.[16]

5. Conclusion

Autologous non-cultured melanocyte transfer is a safe and efficacious modality to produce pigmentation in stable vitiligo patients. It is a novel dermatosurgical procedure which gives decent amount of patient satisfaction in terms of colour match achieved. It has an advantage over conventional grafting in terms of requiring lesser donor area and technicalities. Ideal patient selection, graft harvesting technique and flourished laboratory setup may pose a hurdle in performing this technique. Nonetheless, one cannot condemn the promising nature of this treatment option. Recent large scale studies suggest a propitious role of this procedure in the coming years.

6. Conflict of Interest

There are no conflicts of interest in this article.

7. Source of Funding

None.

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Cite this article: Agrawal M, Varma K, Kumar U, Bhargava S, Gupta S. A study on autologous non-cultured melanocyte transfer in patients of stable vitiligo at a tertiary care centre. *IP Indian J Clin Exp Dermatol* 2023;9(2):61-65.