SUCTION BLISTER GRAFTING- STILL A USEFUL MODALITY FOR TREATMENT OF RESISTANT AND STABLE VITILIGO

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ABSTRACT

BACKGROUND

Vitiligo is a common depigmentation disorder due to absence of functional melanocytes in the affected area. Depending on the type, extent and duration of vitiligo, conventional medical therapies and phototherapy are used. Medical treatment is effective in only 60%-70% of the patients. This has led to the evolution of various surgical modalities to treat recalcitrant stable lesions. The aim of this study was to determine the efficacy of suction blister grafts for treatment of recalcitrant and stable vitiligo.

MATERIALS AND METHODS

This study was conducted on 20 patients with stable vitiligo. They included lip vitiligo (6 cases), segmental vitiligo (6 cases) and focal vitiligo (8) that were resistant to conventional medical treatments. Manual suction with 20 cc disposable syringes for blisters at donor site and dermabrasion at recipient site was done. The blister was separated, fixed at recipient site and dressing was done followed by NBUVB thrice a week for 3 months. Repigmentation of lesions was evaluated monthly for 6 months after treatment. Repigmentation rates > 90%, 71%-90%, 51%-70% and < 50% were graded as complete, good, moderate and poor respectively.

RESULTS

This study includes 20 patients (10 female and 10 male) with stable vitiligo were evaluated for response following suction blister grafting with thrice weekly post-graft phototherapy. Responses to treatment after a 6-month followup were ‘complete,’ ‘good’ and ‘moderate’ in 12 (60%), 6 (30%) and 2 (10%) patients respectively and one patient was lost for followup.

CONCLUSION

The grafting procedures in vitiligo are performed for cosmetic purposes. Proper selection of the patient is the most important factor for achieving a good cosmetic result. Stability of the disease process is the most important parameter to achieve a successful outcome. Suction blister grafting gives excellent cosmetic results with minimal chances of scarring at the donor or recipient sites.

KEYWORDS

Suction Blister Grafting, Vitiligo, Stability, Repigmentation, NBUVB.


BACKGROUND

Around one percent of the world’s population has vitiligo, a disease which causes white patches on the skin. There are a variety of treatments available, most of which are unsatisfactory.(1) Thus, there remains a group that is resistant to all the non-surgical means of treatment or in whom surgical therapy is considered to be more appropriate than medical means and led to the evolution of various modalities of surgical replacement of the damaged melanocytes to treat recalcitrant stable lesions.

These surgical techniques are collectively known as grafting procedures. The choice of the grafting procedure to be performed usually depends upon various factors like the extent or size of the vitiligo lesion to be treated, the site of the lesion, the age of the patient, his/her expectations and social needs, and lastly the expertise of the operating surgeon.(2,3)

The Grafting Techniques in Vitiligo are divided into Two Main Groups-

i) Tissue grafting, and

ii) Cellular grafting (4,5,6) Table 1.

As such vitiligo is hardly a disease of medical significance, but there is more of a social stigma attached to it because of cosmetic reasons.(7) These grafting procedures in vitiligo are performed for cosmetic purposes and the ideal grafting procedure is one that gives the best cosmetic results. Epidermal grafting using the tops of suction blisters has been found to be the most effective surgical procedure.(6)

Proper selection of the patient is the most important factor for good cosmetic result. The factors that need to be considered are the age of the patient, the site of vitiligo, keloidal tendency and most importantly the stability of vitiligo.

Stability of vitiligo simply means that the disease process is no longer active in an individual patient. Clinically, stability is manifested as absence of new lesions, absence of spread of existing vitiligo lesions, and absence of Koebner’s phenomenon. The minimum duration of stability for vitiligo grafting is still a debatable issue with the recommended minimum duration ranging from 6 months to as long as 4 years in different clinical studies.(9,11) Another debatable issue in this regard is that of patient versus lesional stability, but majority of researchers still
favour patient stability over the lesional stability while selecting a patient for vitiligo grafting.

The IADVL task force has defined stability as ‘the patient with no new lesions, no progression of existing lesions and absence of Koebner phenomenon during the past 1 year.'[12] Therefore, the task force recommends that surgery for vitiligo should be performed only in patients with VIDA scores of -1 or 0[13] (Table 2).

Thus, this study was taken for the determination of efficacy of suction blister grafting technique in the treatment of stable (inactive since 1 year) and resistant (in response to conservative treatments) vitiligo.

MATERIALS AND METHODS
This study includes 20 patients with limited vitiligo that was in stable state but resistant to different medical treatments, attending DVL OP of Government General Hospital, Kakinada from July 2014 to June 2017. Suction blister grafting was done with informed consent. The study was approved by Institutional Ethics Committee.

Inclusion Criteria
Patients attending to OPD with vitiligo stable for at least 1 year, non-responsive to medical treatment and willing for suction blister grafting were included in the study with informed consent.

Exclusion Criteria
Patients with either lesion or patient unstable or active vitiligo were excluded.

Study Design
This study is an uncontrolled clinical trial to establish the efficacy of suction blister grafting in the stable and conventional treatment resistant vitiligo lesions.

Statistical Analysis
To analyse the results, descriptive statistical analysis such as mean, standard deviation (SD) and Chi-square test to test the statistical significance between age, gender, site of lesion and stability with repigmentation were done. P-value 0.05 is taken as significant.

Principle
In suction blister grafting, cleavage occurs between the basal cells and the basal lamina of the basement membrane zone and only the epidermal portion of the donor area is grafted. This method is to transfer active melanocytes from donor area to recipient vitiligo lesions through blister induction, separation of epidermis and then transferring it to recipient area. In a few days, melanocytes penetrate into the recipient area and activate to produce pigmentation.[14] Hence, the graft generally acquires the characteristics of the recipient site, thus leading to a better colour match and cosmetic outcome.

Methodology
- All patients were advised to discontinue previous treatments for at least 4 weeks before the grafting procedure to minimise any possible drug effects.
- **Donor Area:** In this study, the donor site was taken from the flexor aspect of the forearm and the anterolateral aspect of the thigh (covered sites are preferred, as pigmented changes can occur at the donor site).
- **Preparation of Donor Area:** On the day of surgery, a donor site with normal skin was selected and cleaned first with povidone iodine and then with normal saline. After surgical cleansing, a topical local anaesthetic (EMLA) is applied as the procedure is painful.
- **Raise of Blisters:** The device used for inducing a blister consisted of 20 and 50 mL syringes, three-way cannulas, a pressure gauge. 20 mL disposable syringes were used as suction cups. The piston of 20 cc syringe is removed and 3-way cannula is attached to its needle end piece. The basal rim of this 20 cc syringe is then applied to the fully stretched donor site. Suction was attempted by means of a 50 mL syringe attached to the opposite end of the 3-way cannula. Vacuum was retained by locking the suction syringe at the end of the three-way cannula. Once the desired pressure was attained, the suction syringe end was locked. Due to the negative pressure inside the basal rim of syringe, it remains adherent to the donor site in a vertical position along with the attached 3-way cannula. Multiple such 20 cc syringes (8 - 10 or more) can be applied similarly next to each other as per the area of recipient site required to be grafted. Negative pressure is retained for 1 - 2 hours. Time required for separation is 45 mins. to 2 hours.
- **De-roofing the Blister:** Once the blisters are well formed, the roofs of the blisters are gently cut using scalpel blade and was put in a normal saline containing petri dish with roofs everted onto a glass slide, such that the dermal side faces upwards. The graft is then cleaned, spread to its maximum size and smeared with antibiotic cream which prevents wrong placement of epidermal side and infection. Always keep the graft moist with normal saline.
- The donor site was dressed with antibiotic ointment and vaseline gauze.
- **Recipient Site:** While dressing the donor site, another person prepares the recipient site for grafting. The site (vitiliginous macule) is surgically cleansed and anaesthetised with 1% lignocaine. The site is dermabraded using a motor dermabrader till minute pinpoint bleeding spots are visible and dermabrasion is done 1 – 2 mm beyond the vitiliginous area.
- **Transfer of the Graft:** Over the dermabraded recipient area, the glass slide with graft is inverted such that the dermal side of the graft is in contact with recipient area. Each graft is transferred individually, so that a gap of 0.5 cm is left between two grafts for pigment spread. Graft is placed such that edges extend 1 – 2 mm beyond the vitiligo area.
- **Dressing:** To prevent the chance of misplacement of the graft wet sterile cotton was placed over the area, covered with sterile gauze and then firmly bandaged with Dynaplast.
- **Postoperative Care:** After surgery, a week’s course of oral antibiotic (Cefixime 200 mg BD) was given and the patient was instructed to keep the grafted site immobile for a week.
Dressing over recipient area was changed after a week, but dressing over donor area was removed next day and cleaned daily. Scaling of the site was observed as the graft fall off in 1 - 2 weeks.

**Follow-Up:** The patient was asked to come for NBUVB from the day of removal of the dressing for thrice a week for at least 3 months.

- Repigmentation of lesions was evaluated monthly for 6 months after treatment.
- Grading of repigmentation rates > 90%, 71% - 90%, 51% - 70% and < 50% were as complete, good, moderate and poor respectively.

**RESULTS**

20 patients (10 female and 10 male) with stable vitiligo were evaluated for response following suction blister grafting with thrice weekly post-graft phototherapy. The mean age of male patients and female patients in this study was 27.7 ± 3.26 and 22.4 ± 3.33 respectively. The mean period of stability of lesions (in terms of months) in this study was 14.5 ± 2.6. Statistical analysis is done by Chi-square test to test the statistical significance between age, gender, site of lesion and repigmentation. There is statistically no significant difference in repigmentation between male and female (Table 3), stability (months) and repigmentation (Table 5), site of the lesion and repigmentation (Table 6) and age and repigmentation (Table 7).

Initial signs of repigmentation were noticed after 4 - 6 weeks. After 6 months of followup, complete repigmentation (> 90%) occurred in 12 patients and repigmentation of around 90% - 71% is seen in 6 patients, repigmentation of 70% - 51% in 2 patients. The response to treatment after 6 months of follow-up is represented on clinical basis as moderate, good and complete responses were found in 10%, 30% and 60% of patients respectively in Table 4.

<table>
<thead>
<tr>
<th>Gender</th>
<th>Complete</th>
<th>Good</th>
<th>Moderate</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>M</td>
<td>6</td>
<td>3</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>F</td>
<td>6</td>
<td>3</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>12</td>
<td>6</td>
<td>2</td>
<td>20</td>
</tr>
</tbody>
</table>

**Table 3. Gender- Repigmentation**

NS- Nil Significant.

<table>
<thead>
<tr>
<th>Repigmentation</th>
<th>Percentage</th>
<th>No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete</td>
<td>&gt;90%</td>
<td>12 (60%)</td>
</tr>
<tr>
<td>Good</td>
<td>71% - 90%</td>
<td>6 (30%)</td>
</tr>
<tr>
<td>Moderate</td>
<td>51% - 70%</td>
<td>2 (10%)</td>
</tr>
<tr>
<td>Poor</td>
<td>&lt;50%</td>
<td>-</td>
</tr>
</tbody>
</table>

**Table 4**

NS- Nil Significant.

<table>
<thead>
<tr>
<th>Stability (Months)</th>
<th>Repigmentation</th>
<th>Total</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>7</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>15</td>
<td>1</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>18</td>
<td>4</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>12</td>
<td>6</td>
<td>2</td>
</tr>
</tbody>
</table>

**Table 5. Stability (Months)- Repigmentation**

NS- Nil Significant.

<table>
<thead>
<tr>
<th>Site of the lesion</th>
<th>Repigmentation</th>
<th>Total</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior aspect of chest</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Dorsum of right foot</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Forehead</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Left forearm</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Left leg</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Lower lip</td>
<td>5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Posterior aspect of right ear</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Right forearm</td>
<td>0</td>
<td>1</td>
<td>0</td>
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<tr>
<td>Right leg</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Right side of neck</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Right thigh</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>12</td>
<td>6</td>
<td>2</td>
</tr>
</tbody>
</table>

**Table 6. Site of the Lesion- Repigmentation**

NS- Nil Significant.
DISCUSSION
Vitiligo is a fairly common pigmented disorder of skin resulting from a loss of melanin which causes depigmented skin, mucous membrane, eyes and sometimes hair bulbs. The cause of melanocyte destruction has remained unclear,[15] but several theories have tried to explain the pathogenesis of vitiligo such as autoimmunity,[16] self-destructing mechanisms,[17] neural,[18] biochemical,[19] an imbalance of epidermal cytokines[20] and genetic factors.[21]

Vitiligo is not a life-threatening disease; however, it frequently induces emotional distress.[22] Vitiligo should initially be treated with medical therapy. When the therapy fails in spite of all appropriate interventions, surgical treatment may be indicated.[23] Njoo et al recommended a surgical technique as first line treatment of segmental vitiligo and vitiligo involving lips and finger tips.[24] The site of lesions also determines the degree of success of surgical treatment. For instance, the success rates of vitiligo treatments on finger and elbow are considerably lower than those on other sites. The patient’s motivation is also an important factor to be considered.[25]

Autologous skin grafts can be obtained from uninvolved skin using several techniques including a number of dermatorraphy techniques.[26] Each method has its advantages and disadvantages. Suction blister grafting is an effective, non-scarring, surgical repigmentation method that has become popular since 1971 when Falabella first described its use in leukoderma.[27] Suction blister grafting is accomplished by suction of viable epidermis from dermis and pigmented epidermis is used for coverage of achromic areas. Essentially, this is a technique of melanocyte transfer.

At the recipient site, separation of epidermis from the underlying dermis is done till pinpoint bleeding is seen, which is approximately at the dermo-epidermal junction. Removal of the epidermal layer permits plasmatic imbibition for the first 24 to 48 hours and then thereupon vascular ingrowth provides cellular nutrition.[28] In most of the studies in the literature, after completion of epithelialisation (i.e. usually after 1 week) phototherapy was used to induce proliferation and migration of melanocytes in the recipient sites.[29-31] The repigmentation rate in these studies according to the review by Njoo et al was 87%, whereas Ozdemi et al reported rates between 25% - 65%.[29-36] In the study by Maleki et al, ten patients with refractory vitiligo who were treated by suction blister graft and subsequent PUVA therapy reported over 90% repigmentation in seven patients. In studies of blister grafting followed without phototherapy, i.e. Nanda et al evaluated six patients with resistant eyelid vitiligo reported repigmentation in all cases[37] and in another study by Maleki et al showed excellent results in 70% of patients.[38]

Advantages
Major advantage is as graft is very thin and purely epidermal, so minimal chances of scarring at both the donor or recipient sites with excellent cosmetic results especially for vitiligo over eyelids, lips, areola and genitals. Other benefits are no stuck-on effect, no depigmentation, cost effective, simple and safe technique. More importantly it offers a high mean success rate.[39] Scar formation, keloid, cobblestoning, sinking pits, thick margins and milia formation was much less compared to split thickness grafting or punch grafting.[33]

Disadvantages
It is time consuming, as donor site blistering requires a few hours. In the present study, the time to raise blisters was 3 - 4 hours. Blister formation takes more time and is difficult to perform when the patients are young individuals. The weak dermoepidermal adherence found in aged persons makes the separation easier and faster.[14] The other disadvantages are it is not suitable for large areas, folded areas, palms and soles. Also requires specific attention, as epidermal grafting is very easy to tear or to roll up and leads to failure of repigmentation.

In our present study, suction blister grafting followed by thrice weekly phototherapy with NBUVB outcome was complete response, i.e. more than 90% repigmentation was seen in 60%, good response i.e. about 90% - 71% of repigmentation in 30% and around 10% patients showed moderate response i.e. 51% - 70% of repigmentation.

CONCLUSION
Vitiligo causes photosensitivity, severe cosmetic distress, profound psychological impact, great social stigma and affects the quality of life. Surgical methods of treatment for vitiligo constitute an important adjuvant for patients unresponsive to medical therapy. Proper case selection based on the determination of stability of the lesions is very important. Above all proper patient counselling, both about the nature of the disease and the surgery is essential. Our study shows that suction blister grafting technique followed
by thrice weekly phototherapy is effective, easy, facile and safe for treating stable and limited vitiligo.

Limitations
Our study had limitation of small sample size as many patients were not willing to undergo the procedure considering the pain (accompanying suction blister graft technique), the relatively long time needed for the procedure at present, also patients with larger lesions as they need multiple grafts to cover the lesional area and also those whose disease was in an unstable condition were excluded from the study.

Further studies were needed to get the clear consensus on the efficacy of suction blister grafting. Further research needed for finding methods to reduce pain and shorten the time required for blister induction could be valuable.

ACKNOWLEDGEMENT
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REFERENCES


