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Surgical treatment of vitiligo

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Abstract
Surgical treatments for vitiligo are a safe and effective treatment modality for select patients with vitiligo. Many techniques of vitiligo surgery exist, each with unique advantages and disadvantages. Surgical therapies can be subdivided into tissue grafting methods and cellular grafting methods. Tissue grafting methods mainly include mini punch grafts, suction blister roof grafts, and hair follicle grafts. Cellular grafting methods include cultured and non-cultured treatments.

Keywords: Vitiligo, surgical treatment, tissue grafting, cellular grafting

Introduction
Vitiligo is a skin disease characterized by the chronic loss of functional melanocytes. An international consensus definition has recently classified the disease into segmental, non-segmental, and unclassified types. Segmental vitiligo is less common and usually occurs with a unilateral and band-shaped distribution. Non-segmental vitiligo is characterized by generally bilateral or symmetrically scattering over the entire body [1].

It has been proven that patients with vitiligo present severely lowered self-esteem, which, in turn, affects social behavior and may determine the development of depression, whereby this problem is more often observed among women than men [2].

Due to the fact that vitiligo is the most common hypopigmentation disease, the prevalence of which is estimated at 0.1–2%, depending on the sources, numerous researchers from around the world are trying to improve the available forms of treatment as well as develop new techniques, due to which the therapeutic effect will be able to bring the best possible results. Presently, there are several methods for treating hypopigmentation changes in the course of vitiligo. In the case where commonly used therapies, mainly those based on topical corticosteroids and phototherapy, do not give satisfactory results, surgical treatment should be considered [3].

Vitiligo
Vitiligo is an acquired pigmentary disorder of unknown etiology that is clinically characterized by the development of white macules related to the selective loss of melanocytes [4].

The worldwide prevalence of pediatric vitiligo is 0–2.16% [5], with head and neck involvement being the most common at 36.5% [6].

Generalized non-segmental vitiligo is the most common clinical presentation and often involves the face and acral region and is seen in one third to two thirds of patients [7]. Segmental vitiligo is more common with early onset and can account for almost a third of pediatric cases [8]. Stability in vitiligo refers to the arrest of disease activity and is commonly defined as an absence of new lesions, no extension of pre-existing lesions, and an absence of Koebner's phenomenon (KP) during the past 1 year according to the Indian Association of Dermatologists and Venereologists (IADVL) [9].

Surgical treatments
Surgical treatments offer some of the best results for stable vitalization. Repigmentation can improve by 68% in certain types of vitiligo with only 1 treatment session when repigmentation is obtained in these patients, relapse is uncommon [10].

Indications

Surgical treatment is an excellent option for patients with stable vitiligo who are unable to achieve cosmetically pleasing results with nonsurgical methods. The best indications are stabilized segmental or focal vitiligo, mainly when SV is characterized by leucotrichia and large lesional areas. In NSV various recommendations suggest a period of disease inactivity ranging from 6 months to 2 years, and no history of a Koebner isomorphic response. No consensus exists concerning the minimal age for surgery, which is generally performed under local anaesthesia [10].

Contraindications

The absolute contraindication is keloidal tendencies and hypertrophic scars. Hyperpigmentation in the area of previous injury or burn may be a relative contraindication. However, patients tend to accept hyperpigmentation rather than hypopigmentation. Several surgical options exist, which can be classified into tissue and cellular grafts [11].

Tissue grafts Surgery

1) **Mini punch graft (MPG):** It is performed by placing punch biopsy specimens from a donor site into a prepared recipient site. This procedure is rapid, inexpensive and technically simple. It can be performed on almost all sites especially difficult-to-treat sites, such as eyelid, lips, nipples, palms and skin folds but is difficult to perform on large areas, can lead to pigment and textural variations such as cobble stoning, and carries a risk of scarring and keloids [12].
2) **Epidermal blister grafting:** It involves the formation of epidermal blisters by applying negative pressure to the normally pigmented skin. After blister formation, the depigmented epithelium is removed, and the roofs of the pigmented donor blisters are transplanted to the denuded lesional areas. Suction blister technique (SBT) is convenient and cost-effective, pure epidermal graft, and excellent color match [13].
3) **Split-thickness skin graft:** It is less popular than the blister graft, but it has a major advantage of being able to cover large areas with a single surgical procedure. The graft is harvested with the assistance of a dermatome which creates a graft of uniform thickness. It is then meshed to prevent seroma formation and to cover a greater area. It is placed over a dermabraded recipient site and dressed in gauze [14].
4) **Hair Follicle Grafting:** Re-pigmentation of vitiligo occurs from hair follicle melanocytes. Hence, hair follicle transplantation over a vitiligo patch leads to repigmentation of the patch, especially in hair-bearing areas with leukotrichia. This procedure is based on the concept of the existence of undifferentiated stem cells in the hair follicle, which forms a good source of melanocytes for re-pigmentation [15]

Hair follicle transplantation is scarless surgery, good technique for management of leukotrichia and vitiligo in hairy areas, no cobblestoning, and good color match. But it also requires expertise and time [15].

Cellular grafts Surgery

Cellular grafts can be cultured or non-cultured and involve creating a cellular suspension from a thin to ultrathin skin graft. Non-cultured options, although complex, do not require a full cell culture laboratory. Therefore, non-cultured epidermal suspension (NCES) grafting, also known as a melanocyte keratinocyte transplant procedure, is performed more frequently than cultured melanocyte grafting. It is now considered the criterion standard for vitiligo grafting worldwide [1].

1) Cultured epidermal graft

A shave biopsy of normally pigmented skin is the source for epidermal cell culture. After separating the epidermis from the dermis, the cells are seeded in a medium that allows co-cultivation of melanocytes and keratinocytes. After a few weeks a cultured sheet is obtained, released by treatment with dispase and attached to a petrolatum gauze as support. Subsequently the gauze to which the epithelium adheres will be applied onto the dermabraded recipient site and covered with occlusive dressing [16].

2) Non cultured trypsinised epidermal suspension

NCES is performed by harvesting an ultrathin skin graft from a donor site, which is then incubated in trypsin. After removing the epidermis from the dermis, the epidermis is manually disrupted and then centrifuged to obtain the cellular pellet, which is resuspended in Ringers lactate, applied to the abraded recipient site, and dressed. Movement should be restricted postoperatively to avoid displacement dressing, but bed rest is not required. Dressings are removed between days 4 and 7. This procedure yields good cosmetic results and color match [17].

3) Simplified Non-Cultured Non-trypsinised Epidermal Cell Graft

The Jodhpur technique used by the author is an autologous, non-cultured, non-trypsinised, melanocyte and keratinocyte grafting technique. This technique does not require split thickness graft and there is no need for trypsinisation. It is a simple procedure [18].

The lateral area of the thigh was selected as a donor site for all the patients. Hair at the donor site was shaved off. The donor site was painted with povidone-iodine and then cleaned with spirit and 2% lidocaine was infiltrated. This was followed by the application of antibiotic ointment to get a high yield of epidermal particles. Dermabrasion was done with the help of micromotor dermabrader at slow rpm till pinpoint bleeding was seen. The application of ointment to the donor area helps in preventing spillage of the graft and efficient trapping of the particles. In some cases, manual dermabrader was also used to obtain epidermal cells in the same manner as an electric dermabrader. Dermabrasion then continued till the upper dermis and then stopped. The paste-like material obtained by this procedure containing melanocytes, keratinocytes and dermis was collected with spatula and was subsequently spread over the recipient area. The donor area to be abandoned is one-fourth of the recipient area [18].

The recipient site was prepared in the same manner as the donor site except no harvesting of epidermal particles was done. The paste-like material obtained from donor site which contained epidermal cells was spread over the recipient area as a thin film. Dressing was done with antibiotic-soaked gauze at both donor and recipient sites. After 10 days, dressing at both sites was removed. Both the sites were left without dressing. Patient was advised to apply topical liquid povidone-iodine daily with the help of a

cotton swab, and oral antibiotics were given till complete healing of the recipient and donor site was achieved (14–18 days). Psoralen and ultraviolet A light (PUVA) therapy was initiated 21 days after the procedure whereby 8-methoxypsoralen was applied topically followed by exposure to sunlight. This was done twice a week for a duration of 16–20 weeks [18].

4) Non cultured extracted hair follicle outer root sheath cell suspension (NCEFORS): The idea first came from the clinical observation of repigmentation patterns in vitiligo lesions, which often start around the follicles. This phenomenon is called "perifollicular repigmentation" and suggests the existence of a melanocyte "reservoir" population in the human hair follicle. This phenomenon was studied extensively [19], who identified an amelanotic outer root sheath (ORS) cell population which was negative for the DOPA reaction and contained nuclei that stained densely with toluidine blue and thionine. This population was found to be activated upon excision of the epidermis or by UV therapy. It was proposed that this amelanotic cell population generated DOPA-positive dendritic melanocytes that migrated to the epidermis and were responsible for perifollicular repigmentation [20].

Cui *et al* [21] Found that treatment stimulated these cells to proliferate and migrate upward along the surface of the outer root sheath to the surrounding epidermis, where they resulted in clinically visible repigmentation. Currently, it is well-known that the bulge area of the human hair follicle is found to be a niche of epidermal and melanocyte stem cells.

The bulge area or lower permanent portion of the hair follicle was later identified as the stem cell niche. Melanocyte stem cells were identified and localized to this site in *Dct-LacZ* transgenic mice by Nishimura *et al.* in 2002 [22], who identified *LacZ*-positive cells in the bulge and sub-bulge area of murine hair follicles which produced mature melanocytes during subsequent hair cycles. These *LacZ*-positive cells were small, oval-shaped, and devoid of dendritic processes and melanin pigment, unlike the mature melanocytes. However, they were found to be capable of differentiating into mature pigmented melanocytes. These cells had all the hallmarks of melanocyte stem cells that is, slow cycling, self-maintaining, and an ability to generate differentiated cells. This observation of the bulge region of the follicle as a stem cell niche has had a great impact on pigment cell biology. These findings suggested that inactive melanocytes in the ORS of the hair follicle divide, proliferate and mature during the process of repigmentation, and may potentially be harvested and cultivated for therapeutic purposes in vitiligo. This was the rationale for the innovation of the technique of NCORSHFS cell suspension transplantation for the treatment of stable vitiligo [23].

5) Combination of Follicular and Epidermal Cell Suspension

Novel approach was reported by Razmi *et al* [24]Using combination of epidermal cell suspension and NCEF ORS and it demonstrated significantly better outcome in terms of extent of repigmentation, early achievement of good repigmentation and patient satisfaction in patients treated compared to those treated with only epidermal cell suspension. This was also proved by measuring melanocyte stem cell counts as well as expression of basic fibroblast growth factor and stem cell factor which were found to be significantly higher in the combined epidermal and hair follicle suspension compared to epidermal suspension alone.

Conflict of Interest
Not available

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