ejpmr, 2019,6(5), 600-609

SJIF Impact Factor 4.897

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

GRAFTING OF MELANOCYTE CELL SUSPENSIONS IN TREATMENT OF VITILIGO

Sara Shreen*[1] and Nimrah Bari[2]

[1,2]Department of Clinical Pharmacy, Deccan School of Pharmacy, Hyderabad.

***Corresponding Author: Dr. Sara Shreen**

Department of Clinical Pharmacy, Deccan School of Pharmacy, Hyderabad.

Article Received on 19/03/2019 **Article Revised on 09/04/2019** **Article Accepted on 30/04/2019**

ABSTRACT

Vitiligo is a common condition seen in a dermatology office, which has a variety of comorbidities. Worldwide, the prevalence of vitiligo ranges from 0.4 to 2.0 %, with regions of greater or lesser prevalence. Most studies demonstrate slightly greater prevalence in females and 50 % onset in childhood, but exceptions to these rules exist. Childhood vitiligo has been associated with atopic diathesis, halo nevi, and family history of vitiligo and autoimmunity. Post-pubescent vitiligo has been associated with greater acrofacial disease and thyroid disease, and early data supports reduced non-melanoma and melanoma skin cancer risk. Disease severity is inversely proportional to distance from the equator, and birthplace outside the USA may be somewhat protective against severe disease. This article reviews the epidemiology of vitiligo and the epidemiologic relationship of vitiligo to comorbid diseases and family history, with a focus on recent literature.

KEYWORDS: Dermatology Pediatrics Post-pubescent Comorbid diseases Family history Literature review.

INTRODUCION

Vitiligo is a cutaneous pigmentary disorder caused by selective destruction of melanocytes and is characterized by progressive, patchy loss of pigmentation from skin. Vitiligo is the most common disorder of pigmentation, affecting ~1–2% of the world's population, generally occurring during the second decade of life 1. Clinically, there are two types of vitiligo. Localized vitiligo can be segmental and present in a dermatomal distribution or may be focal and present in an asymmetric distribution involving segments of skin. Generalized vitiligo (GV) is characterized by multiple scattered lesions in a symmetrical distribution. The course of vitiligo has an unpredictable pattern, with progressive and stabilized depigmentation phases. Active vitiligo is defined by enlarging lesions or formation of new lesions.[2] The impact of vitiligo on patients' self-esteem and social interactions can be devastating, particularly when milk-white skin lesions appear in darkly pigmented individuals.[2]

Before investigating the etiology of vitiligo, investigators first had to prove that melanocytes were absent in the patches of depigmentation in vitiligo. Immunostaining with antibodies against different melanocyte antigens supported the loss of differentiated melanocytes from vitiligo lesional skin. In addition, c-KIT staining for undifferentiated melanocyte stem cells showed that vitiligo lesional skin is also devoid of melanocytic precursors.[3]

The exact pathophysiology of vitiligo is not fully understood. There are a few major hypotheses for the pathogenesis of vitiligo.

(i) Autoimmune pathogenesis is a long-standing and popular hypothesis.

(ii) the neural hypothesis suggests that nerve endings release neurochemical substances that can decrease melanin production or damage melanocytes.[1]

(iii) The biochemical hypothesis implicates the accumulation of toxic intermediate metabolites of melanin synthesis[4] and defective free radical defense[5], and the build-up of excessive quantities of hydrogen peroxide (H2O2) as a cause for destruction of melanocytes.[6] Other hypotheses include genetic factors, defects in the structure and function of melanocytes, and deficiency in melanocyte growth factors are playing a role in the depigmentation process.

Not one hypothesis can explain the pathogenesis of vitiligo on its own. The convergence theory proposes that many of the hypotheses play a role in vitiligo. In addition, some hypotheses play a larger role than others in certain manifestations of vitiligo. For example, GV has more supporting evidence for the autoimmune hypothesis, whereas segmental vitiligo has more supporting evidence for the neural hypothesis.[7–11]

Symptoms

The main sign of vitiligo is patchy loss of skin color. Usually, the discoloration first shows on sun-exposed areas, such as the hands, feet, arms, face and lips.

Patchy loss of skin color Premature whitening or graying of the hair on your scalp, eyelashes, eyebrows or beard Loss of color in the tissues that line the inside of your mouth and nose (mucous membranes) Loss of or change in color of the inner layer of the eyeball (retina) Vitiligo can start at any age, but often appears before age 20.

Depending on the type of vitiligo you have, the discolored patches may cover.
Many parts of your body. With this most common type, called generalized vitiligo, the discolored patches often progress similarly on corresponding body parts (symmetrically). Only one side or part of your body. This type, called segmental vitiligo, tends to occur at a younger age, progress for a year or two, then stop. One or only a few areas of your body. This type is called localized (focal) vitiligo. It's difficult to predict how your disease will progress. Sometimes the patches stop forming without treatment. In most cases, pigment loss spreads and eventually involves most of your skin. Rarely, the skin gets its color back.[18]

Pathogenesis
Although the cause of vitiligo is unknown, there are three hypotheses for its pathogenesis including biochemical/cytotoxic, neural and autoimmune: the biochemical/cytotoxic hypothesis emphasizes that vitiligo occurs when the melanocyte is killed by cytotoxic precursors to melanin synthesis; the neural hypothesis is based on nerve injury development with effected sites that leads to segmental vitiligo with neurons that interact with melanocytes and release melanocytotic substrates; the autoimmune hypothesis is based on genetic data which are more associated to autoimmune diseases.[19]

Although these three theories are sufficient to explain the mechanisms of vitiligo, the convergence theory is that stress, accumulationoftoxic compounds, infection, autoimmunity, mutations, altered cellular environment and impaired melanocyte migration and proliferation can all contribute in varying proportions to the etiopathogenesis of vitiligo.[20]

Some evidence emphasizes that vitiligo occurs through autoimmunity. In a study where the lesion, perilesional, and non-lesional skin biopsies from patients with vitiligo were compared with immune infiltrates found in the skin of normal healthy donors and relevant disease controls a major role was observed for skin-homing T cells in the death of melanocytes seen in vitiligo.[21] The family history of vitiligo in 20% to 30% of patient+s makes a chromatic role for genetic factors.[22] However, there is not sufficient data to support the exact cause of vitiligo. might be triggered by conditions other than sunburn, such as viral infections or physical trauma to the skin. The disorder appears to have an autoimmune characteristic, in which melanocytes (melanin producing cells) are attacked and destroyed. Vitiligo usually first appears by the age of 20, though it can begin later.

There are a number of treatments for vitiligo with the best evidence for applied steroids and the
combination of ultraviolet light in combination with creams.[23] Due to the higher risks of skin cancer, the NHS suggests phototherapy only be used if primary treatments are ineffective.[24]

Historical Aspects
Skin grafting was first described in India in ancient Sanskrit texts around 2500 - 3000 BC as a technique for nasal reconstruction for mutilated noses. Thin split thickness skin grafts were first introduced in 1872 by Ollier in France, and later by Thiersch in Germany in 1874. Brown in England developed the electric dermatome in 1944, to harvest thin homogenous grafts. In 1947, Haxthausen transplanted thin split thickness skin grafts from normal to vitiliginous skin in three cases, to study the pathogenesis of the disease.[25,26] In 1964, Behl from India was the first to describe the surgical treatment of vitiligo in a large series of 107 patients with thin Thiersch grafts.[27] Falabella described the suction blister technique for repigmentation of vitiligo in 1971[28] and later the miniature punch grafting technique in 1978.[29] Flabella et al.,[30] in 1989, also described the use of in vitro cultures of melanocyte-bearing epidermis for the treatment of vitiligo. The use of epidermal suspensions obtained by trypsinization was first reported in 1992 by Gauthier and Surleve-Bazeille[31] and further improved by Olsson and Juhlin,[32] by adding a melanocyte culture medium, for additional growth. Kahn and Cohen[33] utilized the motorized dermatome, to obtain ultrathin grafts for vitiligo, and later in 1996 Kahnetal.,[34] reported the use of a short-pulse carbon dioxide laser, to denude the recipient area. Subsequently, the excimer laser and targeted phototherapy have been developed to treat vitiligo. Thus, surgical treatment of vitiligo has evolved over the centuries, even though the etiology and pathogenesis of vitiligo remain elusive.

TREATMENT OF VITILIGO
Therapies

- Combining psoralen and light therapy. This treatment combines a plant-derived substance called psoralen with light therapy (photochemotherapy) to return color to the light patches. After you take psoralen by mouth or apply it to the affected skin, you're exposed to ultraviolet A (UVA), UVB light or excimer light. These approaches tend to have better results than just medication or just light. You may need to repeat treatments up to three times a week for six to 12 months.
- Removing the remaining color (depigmentation). This therapy may be an option if your vitiligo is widespread and other treatments haven't worked. A depigmenting agent is applied to unaffected areas of skin. This gradually lightens it so that it blends with the discolored areas. The therapy is done once or twice a day for nine months or longer.

- Side effects can include redness, swelling, itching and dry skin. Depigmentation is permanent, and you'll always be extremely sensitive to sunlight.[35]

Basic Principles

The basic principle of surgical treatment in vitiligo is to achieve cosmetically acceptable repigmentation of the vitiliginous areas by transplantation of autologous melanocytes from the unaffected pigmented skin to the lesional skin. It cannot stop the progression of the disease, and is indicated for resistant stable vitiligo that does not show adequate response to medical therapy. Different surgical modalities are available and the choice of surgical treatment depends on the type of vitiligo, extent and site of the lesions, and the availability of equipment and expertise of the treating surgeon.

Concept of Stability in Vitiligo

Stability of the disease process in vitiligo is the most important parameter to achieve a successful outcome in surgical treatment. Stability is defined as the absence of new lesions and absence of the spread of existing lesions for a defined period. However, there is no consensus on the period of stability.and it varies from 4 months to 2 years, according to different authors.

Indications: Surgery in vitiligo is indicated in patients with stable vitiligo not responding to medical treatment or causing severe psychosocial distress. It can also be performed in patients with leukoderma due to burns, piebaldism, inactive discoid lupus erythematosus, and other stable disease states causing permanent depigmentation.

Surgery in vitiligo is indicated in patients with stable vitiligo not responding to medical treatment or causing severe psychosocial distress, causing permanent depigmentation**.**

Contraindications

Vitiligo surgery is contraindicated in patients with active unstable vitiligo, ie vitiligo that progress over a period of 6–12 months. and in childhood vitiligo. In children, progress of the disease is difficult to predict and by and large they respond better to medical therapy as compared to adults. In addition, surgery has to be carried out under general anesthesia, which is another added risk factor in children.[36],[37],[38],[39]

Epidemiology

Prevalence and Epidemiology

Commonly it is stated that about 1% of the world's population has vitiligo vulgaris and that this prevalence is constant for all ethnic groups in all countries; however, the extant data do not confirm these assumptions. Several large studies have been done in Denmark and in India that suggest the prevalence is much lower than frequently purported. In 1973, an investigator reported the results of an extensive survey of both urban and rural populations in or around the city of Surat, India.1 He and his colleagues examined 1887 rural inhabitants and 7178 residents of the city. These ascertainment groups represent about 60% of the population of the area. He observed that vitiligo vulgaris affected 0.49% (1 per 212 individuals) in the rural areas. The prevalence was higher in the urban areas. He found that 1.78% or 1 per 56 individuals within the city of Surat had vitiligo. Men and women were equally affected, although members of certain castes or tribes had higher or lower prevalence rates than the population at large. Some castes had no affected members, others as many as 3.6%. Kinships tended to express a vitiligo trait, so that often two or three members of the primary kinship (parents, siblings and children) were affected; however the familial patterns did not conform to any obvious Mendelian trait. Another investigator studied 15,865 individuals in Calcutta, India drawn from the general population.2 He found the general prevalence of vitiligo in Calcutta to be 5 per 1000 population, or 0.2%. From those with vitiligo in this group, he ascertained additional pedigree data on the familial patterns of vitiligo. He found additional 270 individuals with vitiligo in the families of the probands in the original study group. Both sexes were equally affected. There was a 4-5-fold increased prevalence of vitiligo within close biological relatives of probands with vitiligo, compared to the population at large.2 In Denmark an investigator surveyed 47,033 Danish individuals for vitiligo vulgaris. He ascertained his subjects by examining medical records, autopsy and hospital charts, and newspaper advertisements. He found that 0.38%, or 1 per 263 individuals, had vitiligo. Both sexes were equally affected. Before the age of 10 years only 0.09% of the population was affected; but the prevalence was maximum by age 60 years, at which time 0.9% of individuals were affected. '? From these studies, it seems reasonable to conclude that the general prevalence of vitiligo vulgaris through- out the world is about 1 per 200 individuals, and that both sexes are affected equally; however it should be noted that there are locations in the world, such as isolated villages in India, where the prevalence can be much higher, as high as 8%.-2 The most obvious explanation for this uneven distribution of vitiligo is inheritance of the disease; however there are workers who are exposed to chemicals that cause them to develop occupational depigmentation that resembles vitiligo.5 It is possible, especially in underdeveloped countries such as India that are burdened by a caste system, that the higher than expected prevalence is related to environ- mental factors or, more likely, to a combination of genetic and environmental factors

Different types of vitiligo surgery:

All types of surgical treatment aim to transfer melanocytes (pigment-producing cells) from normal skin (the donor site) to the skin affected by vitiligo.

Surgical treatment for vitiligo can be considered in two main categories:

- Grafting of melanocyte-rich tissue (tissue grafting)
- Grafting of melanocyte cells (cellular grafting).

Commonly used surgical techniques for regimentation surgery are listed below

Types of vitiligo surgery	
Grafting of melanocyte-rich tissue	**Grafting of melanocyte cell suspensions**
Miniature punch grafting (MPG)	Autologous non-cultured epidermal cell suspensions
Suction blister grafting	
Split thickness skin grafting	Cultured melanocyte suspensions

The superficial or uppermost layer of affected skin is usually removed under local anaesthesia in an outpatient setting. Techniques to remove the skin include.

- Dermabrasion
- Cryotherapy
- Shave biopsy
- Punch biopsy
- Laser therapy

I. Grafting of melanocyte-rich tissue

Miniature punch grafting

Miniature punch grafting is one of the most commonly used techniques, due to its simplicity and efficacy. Bits of skin about 2 mm in diameter are punched out from the donor site on buttock or thigh and placed on the donor site of vitiliginous skin, where recipient chambers have also been created by punches**.**

Procedure

After proper assessment of the stability status, routine physical examination and investigations, an informed consent is taken from the patient. The donor and recipient areas are surgically prepared.

The instruments required are 1.5 or 1.2 mm punches, small jeweler's or graft holding forceps and small curved tip scissors 2. Recipient area is prepared first. Two percent lignocaine with or without adrenaline is infiltrated as local anesthetic. To minimize the chance of developing any peri grafthalo, the initial recipient chambers are made on or very close to the border of the lesion. The punched out chambers are spaced according to the result of TG or at a gap of 5–10 mm from each other. The donor area is either upper lateral portion of thigh or gluteal area. Punch impressions are made very close to each other so that from a small area maximum number of grafts can be taken. Same sized punches are used for both donor and recipient area. The grafts were placed directly from donor (buttock or upper thigh) to the recipient areas. This speeds up the procedure and lessens the chance of infection.

Care is taken, so that the graft edges are not folded, the tissue is not crushed or placed upside down. The needle of the syringe or the tip of the scissors is used for proper placement of grafts in the recipient chambers.

Hemostasis is achieved by pressing a saline soaked gauze piece over the area.

For the recipient area three layers of dressing from inside out were: paraffin-embedded nonadherent sterile gauze (Jelonet®), sterile Surgipad ® and bio occlusive Micropore® For the donor area only Surgipad® and Micropore ®are used.

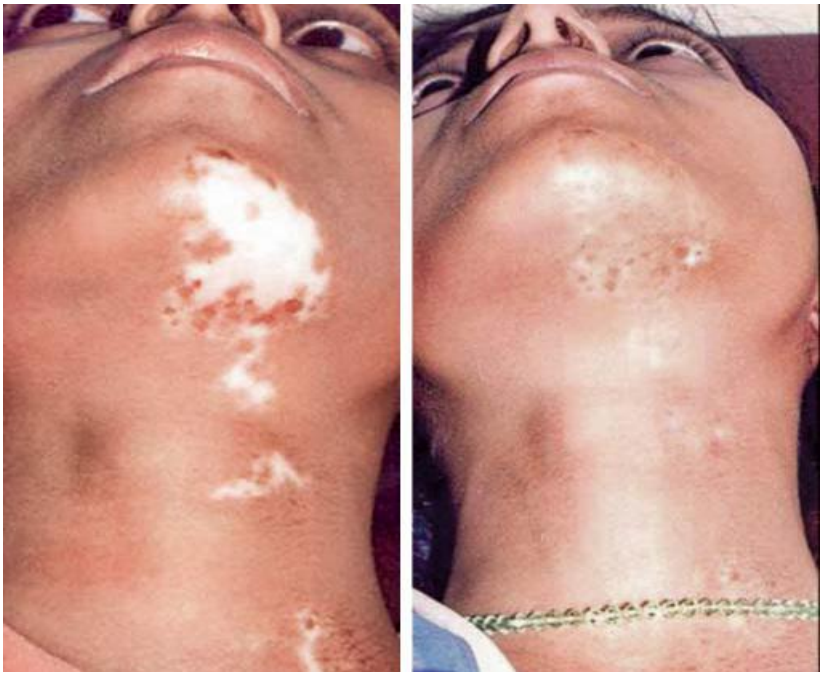


Fig 1 mini punch grafting before and after surgery.

Suction blister grafting

In suction blister grafting, negative pressure is applied to the normally pigmented donor site to promote the formation of multiple blisters.

Blisters may be raised using one of the following options:

- Syringe
- Suction pump
- Suction cups
- Negative pressure cutaneous suction chamber system

The bases of syringes of sizes 10 ml and 20 ml are coated with vaseline and are applied on the donor site. It usually takes 1.5 to 2.5 hours for the development of blisters. The roofs of the blisters (the grafts) are surgically removed, cut to the appropriate size and shape, and transplanted onto the prepared recipient site.

Good cosmetic results can be achieved, with minimal scarring of the donor site or cobblestoning at the recipient site. Suction blister grafting is generally safe, easy to perform and inexpensive, with good success rates. However, it can also be very time consuming, and can be performed only on small area of the skin.

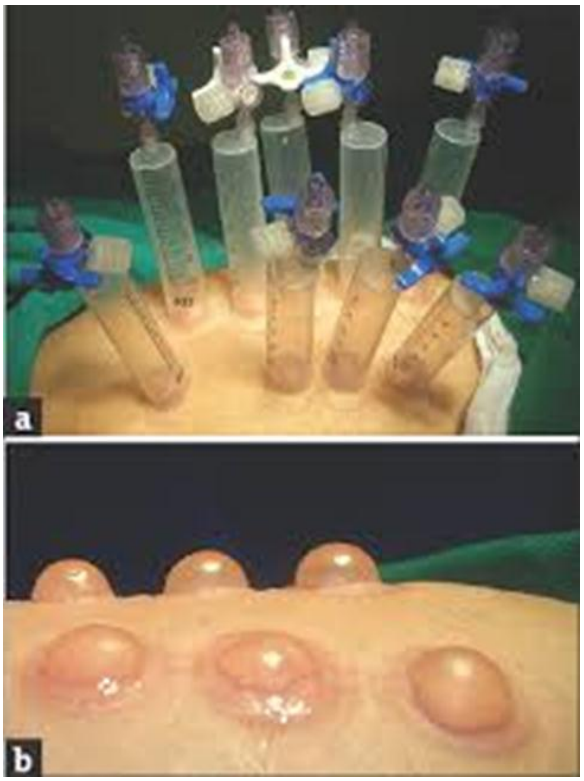


Fig 2- suction blister grafting method

Split thickness skin grafting

Split thickness skin grafting involves shaving off thin layers of skin from the donor site. In comparison to punch grafting and suction blister grafting, split thickness skin grafting can cover larger areas and produces uniform pigmentation with no cobblestoning.

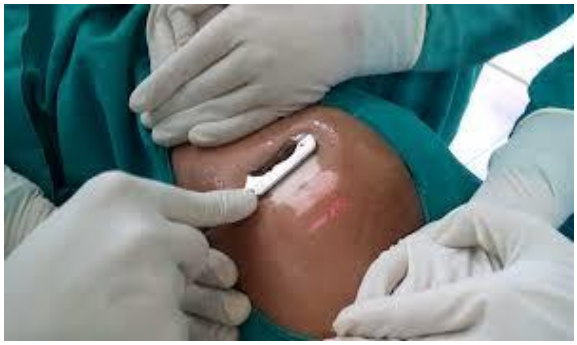


Fig 3: split thickness skin grafting surgery.

Grafting of melanocyte cell suspensions

Autologous non-cultured epidermal cell suspensions

Autologous non-cultured epidermal cell suspensions are gaining popularity around the world as the treatment of choice for surgical management of vitiligo. Pre-prepared kits are available.

Tissue is harvested from a donor site and is incubated with trypsin to separate the epidermis from the dermis. The melanocytes are then separated from the epidermis and made into a cell suspension that can then be transplanted onto the de-epithelialized recipient skin.

Autologous non-cultured epidermal cell suspensions allow large areas to be treated in one session using a small donor graft. They result in excellent colour matching. However the procedure is expensive and complex. Due to stringent rules regarding tissue handling in Australia and elsewhere, it is not yet widely available.

Cultured melanocyte suspensions

With cultured melanocyte suspensions, tissue is also harvested and incubated with trypsin. However, after separation of the epidermis, the melanocytes and keratinocytes are incubated in a medium containing growth factor. The cultured suspension is then transplanted on to de-epithelialized recipient skin.9.[45]

Cultured melanocyte suspensions

Cultured melanocyte suspensions allow a large area to be treated in a single session. It uses a larger donor-to-recipient ratio than the non-cultured technique. This sophisticated technique requires a special laboratory.

Donor area

upper and anterior region of the thigh pre-operative conditions: In the donor area, antisepsis with chlorhexidine and anesthesia was given [local infiltration of 2% lidocaine.

Procedure

The donar site was disinfected with providine, iodine and alcohol and then anesthetized with 1% xylocainwithout epinephrine. A spit thick biopsy of about 1/10 the size of the area to be covered was taken from the inner thigh region of the leg. A 200µm- thick sample was obtain with an electrodermatome 4 and transferred to cell

culture laboratory in a petri dish with strile saline solution to obtain cells. The donar site was covered with strile dressing and mupirocin ointment for seven days.

The sample was transferred to a petridish and washed twice with Dulbecco's modified Eagle Medium (DMEM) and then transferred to a petridish with 4 ml 0.2 % trypsin was added. The sample was checked that epidermis was facing upward, and then incubated for 15 min at 37ºC with 50% CO2 and 95 % humidity. The dermis was separated from epidermis and transferred to test tube containing 3 ml of DMEM and was mixed for 15 sec.the epidermis was washed into small pieces into petri dish washed with DMEM medium and transferred to a test tube with the same medium. The sample was then centrifuged for six min to separate the melanocytes and keratinocytes which sinks to the bottom from the other epidermal cells which floats in the medium was discarded. the cells in the cell pellet was resuspended in a syringe with disposable needle in 500µl/ 1 ml of saline solution, depending on the areas to be treated.

The area to be treated with disinfectant with providine, iodine and 70% ethanol and then anesthestized with 1% xylocaine 4.

The area to be treated will be marked. the ideal point is where some blood spot can be observed the area was covered with a gauzed soaked inn a saline. After removal of the gauze the cell suspension was applied and hen covered with a transparent polyurethane dressing and coated with the chemically inert acrylic adhesive. The dressing was removed after 1 week of transplantation.[46]

MEASUREMENT OF THE REPIGMENTATION

The main parameter of the efficacy was measured in the percentage of repigmentation of the treated area, which was evaluated by measuring maculae or patches at the baseline and three to one year after implantation. Size of each macule was evaluated by iconography and the image was analysed using computer program e to measure the area of lesion in cm^2.[47]

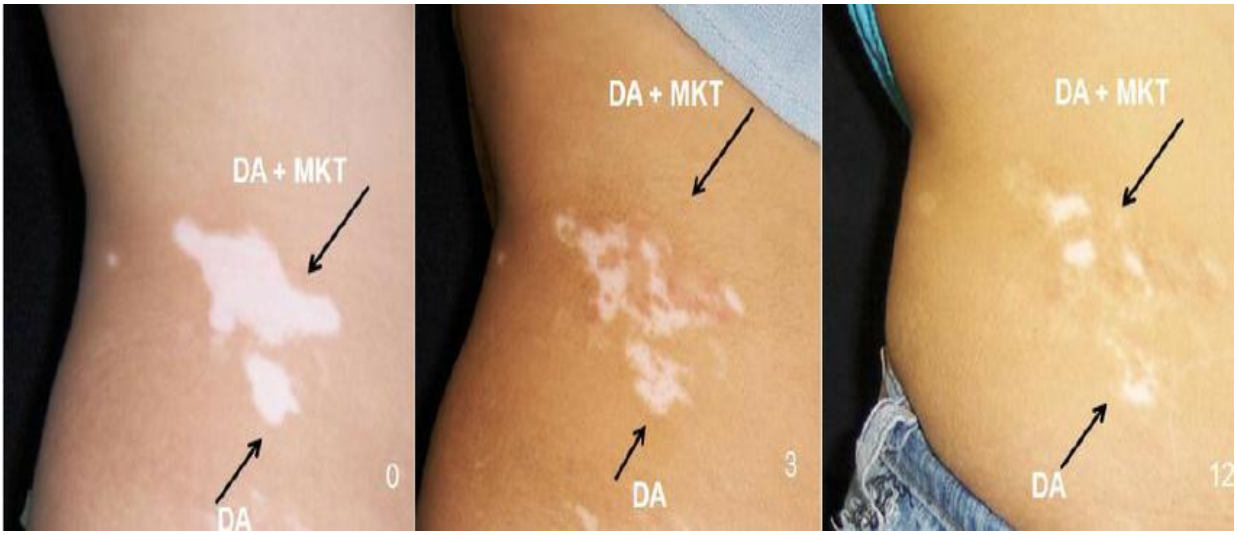


Fig 4: Repigmentation with dermabrasion (DA) and dermabrasion + melanocyte—keratinocyte cell transplantation (DA+MKT) at zero, three and 12 months.

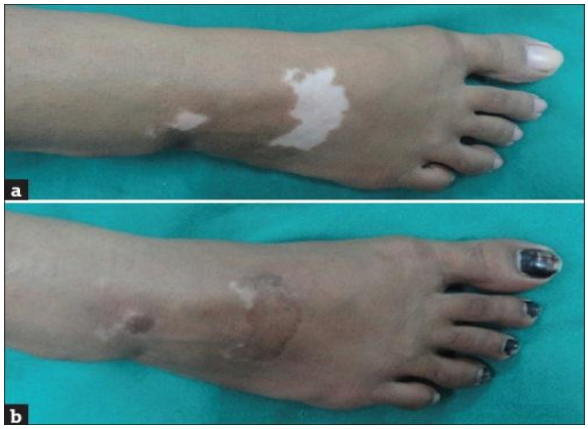


Figure 5: Group A response to epidermal melanocyte transfer over foot. a) Before treatment, b) Patches showing > 90% pigmentation 6 months after treatment.[47]

Autologous non-cultured epidermal cell suspensions:

The skin was stretched and a thin layer (approximately 200µm) was removed by shaving with a flexible blade. A Cicaplast Baume B5 (Niacinamid 4% and Glycerin 30%,) cream was applied on the surface of the wound, which was covered with a gauze and micropore surgical tape. The thin layer of skin was transferred to a Petri plate, with the epidermis turned right side up, containing approximately 4mL of 0.2% trypsin solution and EDTA, and was incubated for approximately 20 minutes in an incubator at 37(o) C. The trypsin solution was then discarded, and the skin sample was washed in DMEM F12 medium. The dermis was separated from the epidermis using delicate anatomical tweezers and fragmented into small pieces. The solution with skin fragments in DMEM F12 medium were transferred to a 15mL tube and centrifuged at 1200 rpm for 6 minutes to obtain a cell pellet. The pellet was re-suspended in a

DMEM F12 medium in a 1mL syringe. The volume was chosen according to the size of the area to be treated, varying between 0.1 and 0.5mL. The receptor area received the application of a topical anesthesia (4% HCL Tetracaine, 4% HCL Lidocaine, 4% HCL Prilocaine in a cream vehicle, Equilibrium pharmacy) 30 minutes before the beginning of the procedure. The receptor area was submitted to dermabrasion with an electric dermabrasion device. The prepared cell suspension was spread uniformly with a 1mL syringe through the entire receptor area after the gauze was removed and was covered again with a collagen dressing. The dressing was then finalized, using sterilized gauze, transparent adhesive dressing and fixed with micropore surgical tape.[49]

Autologous non-cultured melanocyte–keratinocyte transplantation procedure (MKTP) is one of the simplest cellular grafting techniques. Various modifications were done over the years to make the technique easier and more economical which led to its great popularity among dermatologists. Proper patient selection and good technical skills are essential for achieving success with this technique. In this review, different patient-related and procedure-related factors that affect the outcome are discussed. This review may guide dermatologists to select suitable candidates, and explains what to expect in each case and indicates different techniques which can be used.[50]

Preoperative Consultation

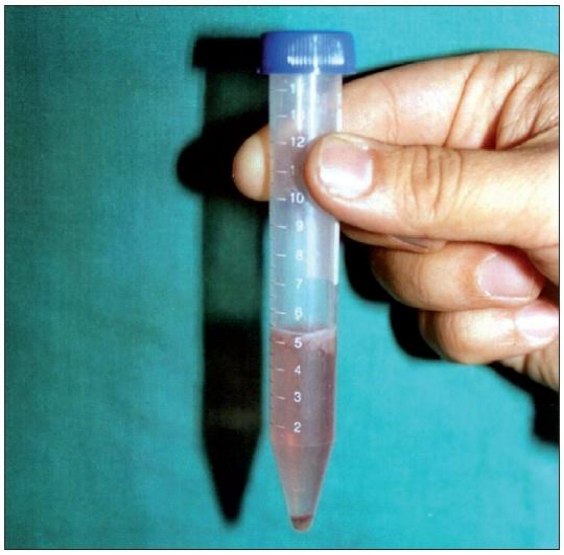
- Proper counseling must be done; the nature of the disease, procedure, expected outcome and possible complications should be clearly explained to the patient.
- Patients should understand that proper results may take time to appear (few months to one year). The patient should be provided with adequate opportunity to seek information through brochures, computer presentations, and one-to-one discussions.
- Obtain the Consent was obtained from all the patients and the risks of, benefits should be discussed

Donar Site

Select about one – tenth of the recipient area, as the donor site, usually on non-cosmetically important sites like the thigh, buttocks and waist. Cleaned with providone iodine (Betadine) and 70% ethanol and drape. Anesthethetized the site with 1 % lidocane infiltrated in the subcutis. Stretch the skin to obtain with the help of silver's skin grafting knife or sterile razor blade on a straight hemostat forceps and dress the superficial wound /In cases having multiple scattered small patches, larger donor skin was taken - approximately one-fifth of the recipient area. Under aseptic precautions, a very superficial sample was harvested using a shaving blade held in straight Kocher's forceps. The donor area was dressed with a liquid paraffin dressing tulle (Fairlee™) and sterile gauze pad.

Cell Separation Technique

The cell separation was done under aseptic precautions in a laminar flow bench kept in the operation theatre. The skin sample harvested was transferred to a Petri dish containing. The epidermis was separated from the dermis and transferred (epidermis) to a test tube containing Nutrient medium The epidermis was further broken into smaller pieces in a Petri dish and washed The epidermis was suspended in a test tube containing Nutrient medium.



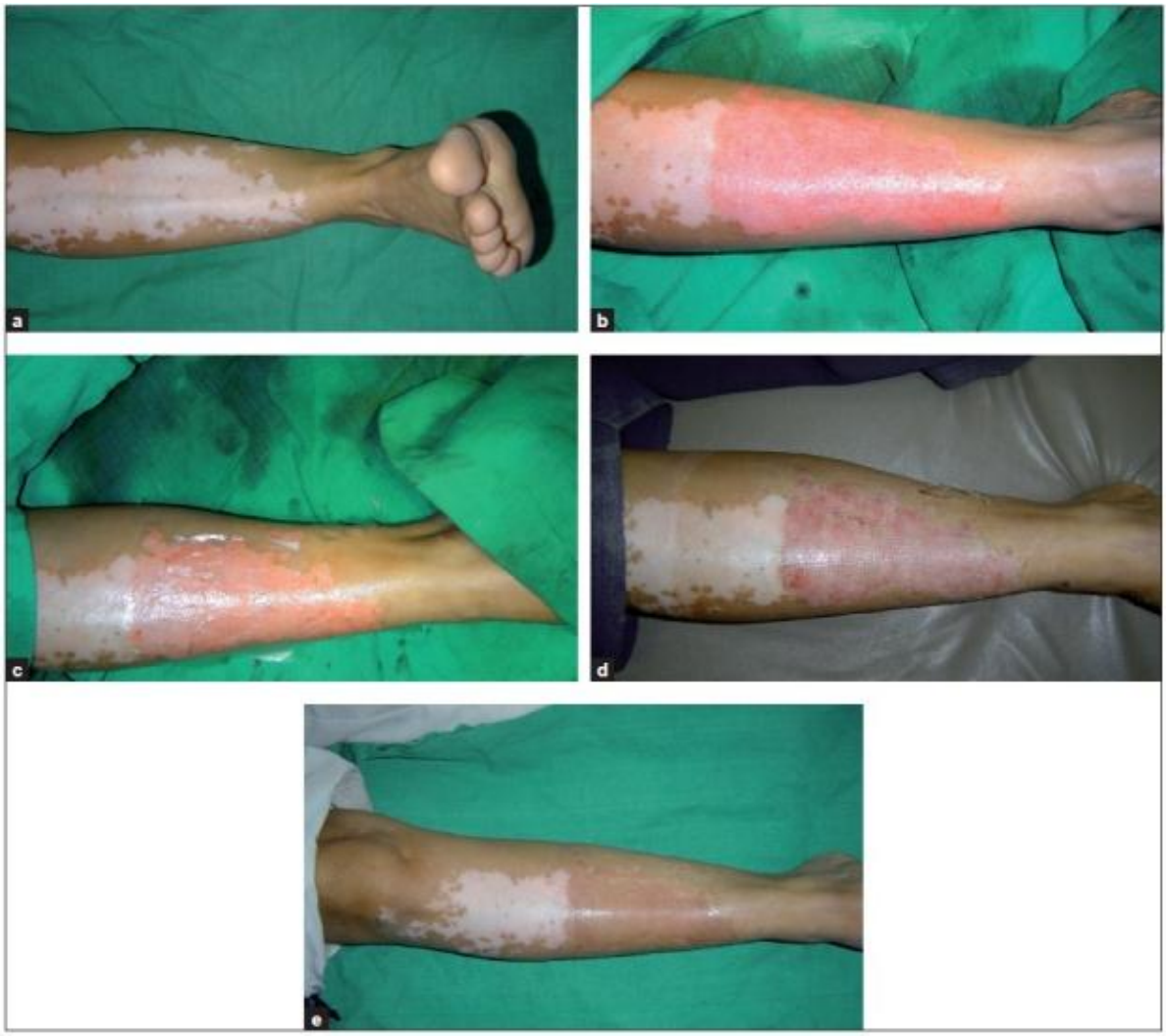
Transplantation technique

The recipient site was abraded with a dermabrader. The endpoint of ablation was pinpoint bleeding. Haemostasis was achieved and the ablated area was covered with saline-soaked gauze pieces. The cell suspension was spread evenly on the dermabraded area and covered with collagen dressing to hold the cells applied. This was covered with liquid paraffin and gauze pieces. Patients were instructed to lie still in the same position for at least 1 h to ensure cell fixation and then shifted to a room and further instructed to avoid excessive movements of the treated area for at least 6 h.

Post-procedure instructions

The dressings were removed after 1 week in most cases. Patients were asked to follow up at weeks 1 and 3, and then at 3-month intervals. Patients were asked to report immediately if they noticed any fresh patches of vitiligo. Patients who had incomplete repigmentation were reoperated after an interval of 6 months only if vitiligo was still stable**.**

The response to the procedure was graded as excellent if the repigmentation was more than 90%, good if the repigmentation was 70–89%, fair if the repigmentation was 30–69% and poor if the repigmentation was less than 30%.[51]



Measurement of repigmentation

Using a Mexameter, MIs were obtained from lesions and symmetrically located control skin. RMIs, ratios of the MIs of lesional skins to control skins, were calculated.[52]

The C+K probe devices are modular and can be put together according to your needs. They consists of a basic device and the probes. Choose a basic device meeting your requirements: with display, only connectable to software or even wireless to transmit the measurement values directly into software. Select the measurement parameters you need for your work. Together, the basic device and the probes will form your individual measurement center.[53]

This study shows that the Mexameter, Skin pigmentation was measured by reflectance spectrophotometer, an objective pigment-measuring device, can be used to achieve a more accurate diagnosis of hypopigmentary disorders, and that the relative melanin index (RMI), which represents the relative pigment levels, might be a more effective parameter than the Melanin content of cultured pigmented cells can be measured by spectrophotometry and expressed either as melanin content per cell or melanin content per culture (area). Melanin content per area is determined by melanin content per cell and the number of cells in this area melanin index (MI) itself for comparing pigmentation differences.[54]

skin analysis software is also available based on melanin measurement function with spectrophotometer. Measurement can be performed by simply placing the head of the spectrophotometer against the skin and pressing the buttom measurement by just applying light to the face, arm or other desired part of the body.[55]

CONCLUSION

Vitiligo, characterized by depigmented macules is a common disorder with a high psychosocial impact. Surgical treatment is indicated in resistant stable vitiligo that does not show adequate response to medical therapy. Stability of the disease process is the most important parameter to achieve a successful outcome. Conventional surgical modalities are tissue grafts such as punch grafting, suction blister grafting and split thickness skin grafts. The choice of surgical treatment depends on type of vitiligo, extent and site of lesions, availability of equipment and expertise of the treating surgeon. Split thickness skin grafting is the most successful out of all tissue grafting methods. Recent advances include autologous non-cultured epidermal cell suspensions and cultured melanocyte suspensions or sheets. Hence though surgical treatment of vitiligo is evolving over the years, the basic etiopathogenetic mechanisms need to be elucidated to achieve long term successful results.

REFERENCES

1. Lerner AB. Vitiligo. Prog Dermatol, 1972; 6: 1–6. Cited Here.
2. Kent G, Al'Abadie M. Psychologic effects of vitiligo: a critical incident analysis. J Am Acad Dermatol, 1996; 35: 895–898. Cited Here... | PubMed | CrossRef.
3. Steel KP, Davidson DR, Jackson IJ. TRP-2/DT, a new early melanoblast marker, shows that steel growth factor (c-kit ligand) is a survival factor. Development, 1992; 115: 1111–1119. Cited Here... | PubMed.
4. Kemp EH, Waterman EA, Weetman AP. Autoimmune aspects of vitiligo. Autoimmunity 2001; 34: 65 77. Cited Here... | PubMed | CrossRef
5. Pawelek J, Korner A, Bergstrom A, Bologna J. New regulators of melanin biosynthesis and the autodestruction of melanoma cells. Nature, 1980; 286: 617–619. Cited Here... | PubMed | CrossRef.
6. Nordlund JJ, Lerner AB. Vitiligo. It is important. Arch Dermatol, 1982; 118: 5–8. Cited Here... | PubMed | CrossRef.
7. Schallreuter KU, Wood JM, Berger J. Low catalase levels in the epidermis of patients with vitiligo. J Invest Dermatol, 1991; 97: 1081–1085. Cited Here... | View Full Text | PubMed | CrossRef
8. Ortonne JP, Bose SK. Vitiligo: where do we stand? Pigment Cell Res, 1993; 6: 61–72. Cited Here...
9. Castanet J, Ortonne JP. Pathophysiology of vitiligo. Clin Dermatol, 1997; 15: 845–851. Cited Here... | PubMed | CrossRef.
10. Norris DA, Horikawa T, Morelli JG. Melanocyte destruction and repopulation in vitiligo. Pigment Cell Res, 1994; 7: 193–203. Cited Here... | PubMed | CrossRef.
11. Le Poole IC, Mutis T, Van den Wijngaard RMJGJ, Westerhof W, Ottenhoff T, De Vries RRP, Das PK. A novel, antigen-presenting function of melanocytes and its possible relationship to hypopigmentary disorders. J Immunol, 1993; 151: 7284–7292. Cited Here... | PubMed.
12. Majumder PP, Nordlund JJ, Nath SK. Pattern of familial aggregation of vitiligo. Arch Dermatol 1993; 129: 994–998. Cited Here... | PubMed | CrossRef.
13. Nath SK, Majumder PP, Nordlund JJ. Genetic epidemiology of vitiligo: multilocus recessivity

cross-validated. Am J Hum Genet, 1994; 55: 981–990. Cited Here... | PubMed.
14. Sun X, Xu A, Wei X, Ouyang J, Lu L, Chen M, Zhang D. Genetic epidemiology of vitiligo: a study of 815 probands and their families from south China. Int J Dermatol, 2006; 45:1176–1181. Cited Here... | View Full Text | PubMed | CrossRef.
15. Alkhateeb A, Fain PR, Thody A, Bennett DC, Spritz RA. Epidemiology of vitiligo and associated autoimmune diseases in Caucasian probands and their families. Pigment Cell Res, 2003; 16: 208–214. Cited Here... | View Full Text | PubMed | CrossRef.
16. Laberge G, Mailloux CM, Gowan K, Holland P, Bennett DC, Fain PR, Spritz RA. Early disease onset and increased risk of other autoimmune diseases in familial generalized vitiligo. Pigment Cell Res, 2005; 18: 300–305. Cited Here... | View Full Text | PubMed.
17. Ting JPY, Willingham SB, Bergstralh DT. NLRs at the intersection of cell death and immunity. Nat Rev Immunol 2008; 8: 372–379. Cited Here... | PubMed | CrossRef.
18. https://www.mayoclinic.org/diseases-conditions/vitiligo/symptoms-causes/syc-20355912
19. Kovacs SO. Vitiligo. J Am Acad Dermatol, 1998; 38(1): 647-66.
20. Le Poole, IC Das PK, van den Wijngaard RM, Bos JD, Westerhof W. Review of the etiopathomechanism of vitiligo: a convergence theory. Exp Dermatol, 1993; 2(4): 145-53.
21. Oakley AM. Rapid repigmentation after depigmentation therapy: vitiligo treated with monobenzyl ether of hydroquinone. Australas J Dermatol, 1996; 37(2): 96-98.
22. Passeron T, Ortonne JP. Physiopathology and genetics of vitiligo. J Autoimmun 2005; 25(S): 63-68.
23. Hitton ME, Ashcroft DM, Gonzalez U. Therapeutic interventions for vitiligo. J Am Acad Dermato1, 2008; 59(4): 713-17.
24. Anon. Vitiligo -treatment. Patient UK. NHS.
25. Falabella R. History and chronology of development of surgical therapies for vitiligo. In: Gupta S, Olsson MS, Kanwar AJ, Ortonne JP, editors. Surgical management of vitiligo. 1st ed. Massachusetts, USA: Blackwell Publishing, 2007; 41–8.
26. Savant SS. Surgical therapy of vitiligo: Current status. Indian J Dermatol Venereol Leprol. 2005; 71: 307–10. [PubMed]