COMPARATIVE STUDY OF PUVA THERAPY VERSUS NARROWBAND UVB THERAPY IN THE TREATMENT OF VITILIGO

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CERTIFICATE

This is to certify that this dissertation entitled "**COMPARATIVE STUDY OF PUVA THERAPY VS NARROWBAND UVB THERAPY IN THE TREATMENT OF VITILIGO**" submitted by **Dr.B.Senthil Selvan,** to the faculty of Dermatology, Venereology and Leprology, The Tamil Nadu Dr.M.G.R. Medical University, Chennai in partial fulfillment of the requirement for the award of MD Degree Branch XII-A (Dermatology, Venereology and Leprology), is a bonafide research work carried out by him under our direct supervision and guidance.

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I, Dr. B.SENTHIL SELVAN declare that the dissertation titled "**COMPARATIVE STUDY OF PUVA THERAPY VS NARROWBAND UVB THERAPY IN THE TREATMENT OF VITILIGO**" has been prepared by me. This is submitted to The Tamil Nadu Dr. M.G.R. Medical University, Chennai, in partial fulfilment of the requirement for the award of MD Degree Branch XII-A (Dermatology, Venereology and Leprology), degree Examination to be held in April 2011.

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This is to certify that the INSTITUTIONAL ETHICAL COMMITTEE of TIRUNELVELI MEDICAL COLLEGE AND HOSPITAL, TIRUNELVELI-11 has unanimously approved the dissertation titled NBUVB AND PUVA THERAPY IN THE TREATMENT OF VILITIGO by DR.B.SENTHIL SELVAN, MD.,(DERMATOLOGY) II YEAR student, TIRUNELVELI MEDICAL COLLEGE, TIRUNELVELI-11 in its meeting held on 09.10.2009.

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To
The Concerned.

SECRETARY
Secretary,
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CONTENTS

INTRODUCTION

Vitiligo is an 'idiopathic' acquired depigmenting disorder characterized by the loss of functional melanocytes from the epidermis. It is the most common pigmentary disorder and it involves complex interaction of environmental and genetic factors that ultimately contribute to melanocytes destruction, resulting in the characteristic depigmented lesions[1].

Vitiligo can be extremely disfiguring, leading to significant patient morbidity. Low self esteem, poor body image and poor quality of life has been found in patients with vitiligo, including significant psychiatric morbidity. This is of particular concern for children and adolescents, as they are in their formative years and developing their sense of self[2].

Vitiligo is perhaps the most frequent depigmenting disorder[3], occurring with a prevalence varying across populations, apparently being less frequent in Caucasians[4] (0.38%), African[5] (0.34%), and Chinese[6] (0.0093%) than in Indians[7&8] (0.46–1.13%). Not so commonly, higher prevalence may appear among isolated populations. Its pathogenesis has been associated with genetic predisposition, autoimmune phenomenon and neural and growth factor dysregulation as well as inherent cellular metabolic defects leading to melanocyte apoptosis.

The phenotypical expression of vitiligo is polymorphic, and several types of vitiligo are distinguished on clinical presentation. The natural course

of vitiligo is gradual, unpredictable and difficult to control. However, sometimes the disease persists in a stable status for a long time.[9]

Vitiligo possess a treatment challenge and will remain so until we find treatments that give consistent, and long-term cure by repigmentation. Several treatment modalities have been advocated including topical therapy with potent topical corticosteroids, calcipotriol, tacrolimus, pseudocatalase therapy and other modalities like melanocyte transplantation, skin grafting, cosmetic camouflage or self tanning preparations and psychological therapy. But these are often unsatisfactory for generalised Vitiligo, for which NB UVB and PUVA are the most important therapies.[10]

In 1974, Parish successfully introduced a treatment combining 8-methoxypsoralen and UVA called PUVA using newly developed Henselar high intensity artificial UVA light. The combination treatment of Psoralen with ultraviolet A (PUVA) therapy is a standardised therapy for vitiligo and is still the mainstay for non segmental vitiligo. Interestingly two-thirds of patients receiving psoralens and ultraviolet light found the treatment worthwhile, meaning that even if treatments are only partially effective, they may achieve psychosocial relief.

The clinical studies with NBUVB in vitiligo are few. Earlier reported studies were mostly done in the western population and the studies in the darker race, including Indians, is limited. Narrow-band ultraviolet B

(NBUVB) is an emerging, effective and safe therapy for vitiligo. It is as effective as PUVA without many side effects. In 1997, Westerhof and Nieuweboer-Krobotova were the first to study the effect of NBUVB in vitiligo. NBUVB therapy has also been reported to be safe in childhood Vitiligo [11].

Recent reports have shown that NBUVB can induce significant repigmentation in either generalized or segmental vitiligo. It inhibits the induction and secretion of cytokines, and stimulates inactive melanocytes in the outer root sheath of hair follicles to proliferate and migrate into vitiligo lesions. In comparing the treatment of vitiligo with NBUVB radiation versus topical PUVA, Westerhof concluded that UVB therapy was slightly more effective, produced faster repigmentation and had fewer side-effects. However, narrowband UVB therapy is not readily available and implies significant start-up expenses.[12]

There are only few studies to compare the safety and efficacy of NBUVB therapy & PUVA therapy in the treatment of vitiligo. More number of studies to compare the same is required. Hence this prospective study is conducted.

AIMS OF THE STUDY

To compare the efficacy and safety of PUVA therapy and NBUVB therapy in the treatment of Vitiligo vulgaris in terms of

- Time taken for initial repigmentation
- Mean grade of treatment response
- Colour match
- Psychological satisfaction
- Side effects

REVIEW OF LITERATURE

HISTORICAL ASPECTS

Vitiligo is a disease that was observed very early in history, and most ancient civilizations and religions had some type of reference about the lack of pigmentation. One of the earliest terms was "Kilas" in the Rig Veda, which means white spotted deer.

The Ebers Papyrus in 1550 BC mentioned two forms of depigmentation that could be interpreted as leprosy or depigmentation resembling vitiligo. By 1400 BC white leprosy spots were called Sweta khushtha in the Atharva Veda.In 1200 BC Japanese Shinto prayers have described depigmentation resembling vitiligo in the book called Amarakosa. Around 600 BC, the Ashtanaga hridaya explained prognostic factors for depigmentation. In 200 BC, the Indian book Manu Smriti described "Sweta Kushtha" meaning "white disease" probably referring to vitiligo.In Tamil Nadu vernacular name “ven Kushtha “ was used from older days to describe Vitiligo.

Years later, the term vitiligo was perhaps derived from the latin word “vitelius” and used to describe the white flesh of calves, and finally the word vitiligo was used by Celsus in his classic Latin book De Medicina in the first Century, Which has become established since then.[13]

EPIDEMIOLOGY

Vitiligo is perhaps the most frequent depigmenting disorder, occurring with a prevalence varying across populations, apparently being less frequent in Caucasians (0.38%)[4], African Caribbean[5] (0.34%), and Chinese[6] (0.0093%) than in Indians[7&8] (0.46–1.13%). Based on some dermatology outpatient records, the incidence is roughly estimated as 3 -4% in India[14.]

Vitiligo may appear at any time from birth to senescence, although the onset is most commonly observed in persons aged 20-30 years. Onset of Segmental type of Vitiligo is usually in childhood within 10 years. Vitiligo is rarely seen in infancy or very old age. The incidence between the sexes follows general population pattern without any particular predilection. A female preponderance has been reported for vitiligo, but it is not statistically significant and the discrepancy has been attributed to an increase in reporting due to cosmetic concerns by female patients.

Vitiligo mostly affects people with skin types III and IV. A higher incidence has been reported among patients with atopic dermatitis.[14]

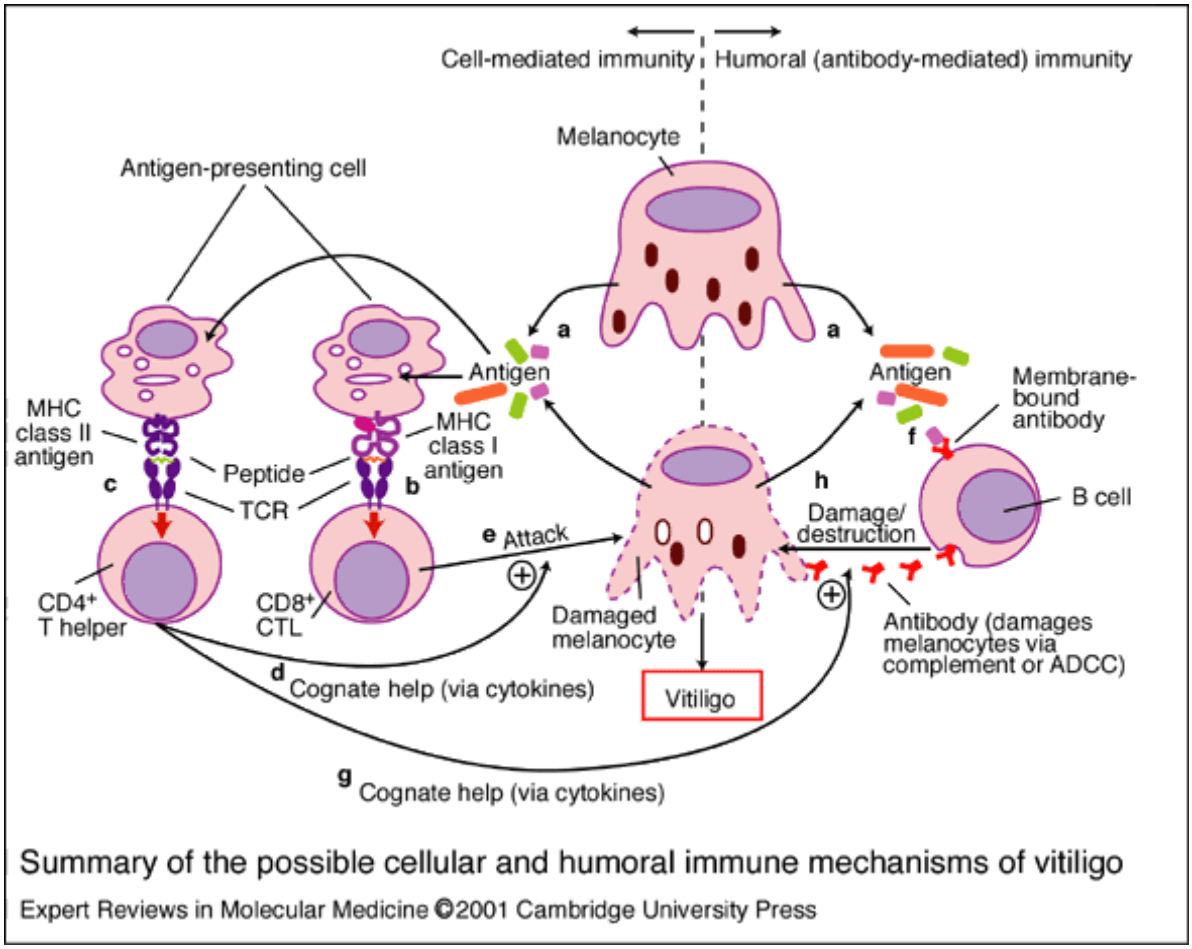
AETIOPATHOGENESIS

Vitiligo is a multifactorial polygenic disorder with a complex pathogenesis. Although several theories have been proposed for the loss of melanocytes in Vitiligo, the precise cause remains unknown. Besides a genetic predilection, diverse epigenic factors also play role in

etiopathogenesis.[14] The Various Theories including autoimmune, cytotoxic, biochemical, anti oxidant and neural have been proposed for destruction of melanocytes. [15]

Autoimmune Theory:

There is great anecdotal evidence that an autoimmune disorder causes the destruction of melanocytes, and this theory is now generally accepted as the common cause of vitiligo. It is known that vitiligo appears in conjunction with several other autoimmune disorders, such as juvenile diabetes mellitus, Thyroid Disease,[16] Addison's disease, and pernicious anemia. Organ-specific antibodies can often be seen in patients with vitiligo. The immune system raises antibodies or cytotoxic T cells to damage melanocytes. Proving this theory, there is histological evidence in vitiligo patients that apoptosis is occurring in the depigmented skin lesions. Some research suggests that the immunoglobulins may bind to tyrosinase related proteins[17] 1 and 2, which are important for melanogenesis.



Summary of the possible cellular and humoral immune mechanisms of vitiligo

Neural Theory:

Peripheral nerve endings may secrete a substance that is cytotoxic to melanocytes and causes their destruction. This theory is supported by the segmental variety of vitiligo, which occurs in specific dermatomes, indicating the skin is possibly only being affected by the nerves of that specific dermatome. Additionally, vitiligo appears with certain neurological disorders such as encephalitis, and trauma that causes peripheral nerve damage.[18] Nerve endings in depigmented areas were seen to produce abnormal neuropeptides and nerve growth factors, and displayed axonal

degeneration-these abnormal chemicals may be toxic to melanocytes. Additionally, depigmented areas showed some abnormal autonomic function, such as increased adrenergic tone, increased norepinephrine, and an increased concentration of catecholamines.[19] These data then suggest that neurotransmitter release could directly or indirectly relate to melanocyte destruction and depigmentation.[20]

Self Destructive Theory:

It is known that some of the intracellular pre-melanogenesis metabolites are toxic to melanocytes, such as dopa and dopachrome. Normally melanocytes possess cellular measures to counteract these toxic substances, but it is believed that cells may lose the ability to counteract these toxic metabolites and are destroyed by leakage of metabolites into the cytoplasm.[15] There is evidence that certain hydroquinone derivatives which are similar to these intra-cellular metabolites cause leukoderma experimentally. [21]

The impaired redox status theory :

Oxidative stress has been suggested to be the initial event in the pathogenesis of melanocyte degeneration with H_2O_2[21][22] accumulation in the epidermis of patients with active disease (12). Defective recycling of tetrahydrobiopterin has been reported in vitiligo epidermis, associated to the intracellular production of H_2O_2[21][23] . In addition, an alteration in the

antioxidant pattern with a significant reduction of catalase activity has been demonstrated in both lesional and non lesional epidermis of patients[21], as well as in melanocytes[22] . However, the antioxidant imbalance has been confirmed also in peripheral blood mononuclear cells of active vitiligo patients; it was correlated to an increased intracellular production of reactive oxygen species and appeared to be due to a mitochondrial impairment[24]. These findings support the concept of a possible systemic oxidative stress in vitiligo.

Growth Factor Defect Hypothesis:

A study in the 1980's found that melanocytes in lesions from Vitiligo exhibited "defective growth and passage capacities." The researchers noted that the growth defects of the melanocytes were partially corrected by adding a growth factor to their culture, suggesting that growth defects may be part of the pathogenesis of Vitiligo. In depigmented areas, cellular analysis showed that there were melanocytes but they grew poorly. These data suggest that growth defects appear to play a role in vitiligo[15]

Genetic Influences:

A positive family history has been reported in about 20% of patients with vitiligo and it has been found in monozygotic twins. Studies have shown that vitiligo does not follow a simple Mendelian pattern, but it is more likely coded polygenically[25]. There has been some evidence both proving

and disproving the involvement of the HLA system in the occurrence of Vitiligo[26]. Several genes and chromosomal regions have been implicated in susceptibility to vitiligo, but none has been confirmed so far[27]. In addition, several HLA abnormalities have been associated with vitiligo, including association with DR4, B13, BW35, and A30[28]. So, it is believed that genetic factors probably play a key role in the pathogenesis of vitiligo, but the exact cause is unknown[15].

Melanocytorrhagy: a newer concept in Vitiligo

It proposes that vitiligo is a primary melanocytorrhagy disorder with altered melanocyte responses to friction and possibly other types of stress, inducing their detachment and subsequent transepidermal loss. Further studies are needed to prove this. Dendrites of melanocytes not only help in melanosomes transfer to the surrounding keratinocytes but also help melanocytes to adhere to basal membrane. Cultured Vitiligo melanocytes show stubby dendrites. Similarly, the addition of H_2O_2 in established cultures of normal melanocytes induces a loss of dendrites and in some cases melanocyte detachment. The increased release of catecholamines might be an aggravating factor of Non Segmental Vitiligo(NSV). It is suggested that in adhesion-deficient NSV melanocytes, dendrites are lost in response to reactive oxygen species or by increased release of catecholamines and exaggerates transepidermal loss. Besides defective adhesion and dendritic

loss, other abnormalities may lead to a decrease in frictional resistance of melanocytes in NSV and eventually to their detachment by mechanical or chemical injury[29].

Convergence Theory:

Following genetic studies, researchers have begun to lean towards a multi-faceted etiology for vitiligo, that combines components of the above mentioned theories and genetics. This theory states that genetic influences have a role in causing vitiligo in addition to other elements, such as stress, accumulation of toxic compounds, infection, autoimmunity, mutations, and impaired melanocyte proliferation[30].

CLINICAL FEATURES

Vitiligo manifests as acquired white or depigmented macules or patches. The lesions are usually well demarcated, sometimes may be ill-defined at the edges and they are round, oval, or linear in shape, rarely irregular. Lesions enlarge centrifugally over time at an unpredictable rate. Lesions range from millimeters to centimeters in size. The most common sites of vitiligo involvement are the face, neck, scalp and areas subjected to repeated trauma including the Bony prominences, extensor aspect of forearm, ventral side of wrists, dorsal aspect of hands and feet[14].

Involvement of the mucous membranes is frequently observed in the setting of generalized vitiligo. Vitiligo often starts around body orifices such

as the lips, genitals, gingiva, areolas, and nipples. Body hair in vitiliginous macules may be depigmented (leukotrichia). Vitiligo of the scalp usually appears as a localized patch of white or grey hair, but total depigmentation of all scalp hairs may rarely occur. Leukotrichia may indicate a poor prognosis with regard to repigmentation. Spontaneous repigmentation of depigmented hair in vitiligo does not occur.

Trichrome vitiligo has an intermediate zone of hypochromia located between the achromic center and the peripheral unaffected skin. This results in three shades of colour - brown, tan, and white. Quadrichrome Vitiligo is another variant of vitiligo which refers to the fourth zone of marginal hyperpigmentation in addition to trichrome vitiligo. Pentachrome vitiligo with five shades of colour has also been described. Marginal inflammatory Vitiligo is Vitiligo patch with a red, raised border which may appear several months or years after the initial onset. A mild pruritus may be present in marginal inflammatory Vitiligo. Blue vitiligo is vitiligo macules occurring in the sites of postinflammatory hypermelanosis[31].

CLASSIFICATION.

Several types of vitiligo are distinguished according to the distribution of the achromic lesions. According to the distribution, extension, and number of white patches, vitiligo is divided into generalized (vulgaris, acrofacial, mixed, and universalis) and localized (focal,segmental, and

mucosal) types[32]. Depending upon the progression, Vitiligo can be classified into stable and unstable Vitiligo[14]

Localized Vitiligo :

1.Focal Vitiligo

Focal vitiligo is characterized by depigmented patch (or a few patches) in a focal and non dermatomal distribution.

2.Segmental Vitiligo

Features of the segmental type include depigmented macules in a quasi dermatomal and unilateral distribution. This type of vitiligo has earlier age of onset and usually stabilizes within a year or two of its onset; it's usually not associated with other autoimmune diseases or a familiar pattern of inheritance.

Generalized Vitiligo:

1. Vitiligo vulgaris - The most common form of Vitiligo has a generalized distribution. This variety of Vitiligo is symmetrical and usually involves the extensor surfaces of the hands, wrists, legs , axillae and offen the face and usually in a symmetrical pattern.
2. Acrofacial Vitiligo - lesion tend to be predominantly distributed on acral parts of limbs, [hands and feet generally the fingers toes palms and soles] and face.

3. Vitiligo Universalis - In this type, the depigmentation is so widespread that only a few areas of normal skinremains

COURSE OF THE DISEASE

The course of the disease is unpredictable and uncertain, most often showing a tendency towards slow progression. Lesions in the pseudosegmental type remain static for an indefinite period after a certain degree of regional extension. In Vitiligo vulgaris, lesions develop on different areas in succession with varying rapidity. In some, extension of individual lesions and development of new lesions at different sites occur in episodic bouts with the intervening quiescent period varying from weeks to years. Many lesions may remain static for an indefinite period or show some degree of spontaneous regression with the development of pigment spots. Others may show repigmentation of some lesions, extension of others, and appearance of new lesions at other sites simultaneously. At times, the pigment spots that occur spontaneously or in response to therapy disappear but may reappear. Complete spontaneous cure is extremely rare. Sometimes residual depigmentation may be left behind after repigmentation.[14]

HISTOPATHOLOGY:

Histopathological examination of vitiligo lesions using melanocyte-specific stains has shown few melanocytes in early lesions and a lack of melanocytes in well-established lesions[31]. In patches with hyperpigmented

borders, the margins were found to contain enlarged melanocytes with elongated dendritic processes containing melanin. A lymphohistiocytic infiltrate along with focal basal layer vacuolar changes has been observed in marginal tissue. Significantly more infiltrate and other inflammatory changes were appreciated in marginal areas and early lesions in one study[33].

VITILIGO THERAPY

Depigmentation in vitiligo should be initially treated with medical therapy. When therapy fails in spite of appropriate interventions, vitiligo may become refractory and stable. Surgical therapy indicated in selected patients with refractory Vitiligo[34].

MEDICAL THERAPY

As a general rule, although not defined by evidence based findings or validated for every medication, topical therapy for vitiligo is usually recommended when depigmentation is less than 10–20% of the skin surface and systemic therapy when exceeding these limits. But when topical therapy of small areas fails, systemic treatment may be indicated. Repigmentation is slow and patients should be advised about compliance and patience

Medical therapy will be divided in the following categories: 1) corticosteroids 2) immunomodulators 3) ultraviolet radiation 4) lasers 5) alternate therapy 6) depigmentation and 7) psychological support and camouflage. Selection of a specific therapy depends on effectiveness

supported by evidence based information and according to the dermatologist's experience since diverse treatments may offer comparable results. Alternate therapy should be tried when therapeutic failures to first line treatments occur[34].

Topical corticosteroids:

This is a first line therapy for localized vitiligo,. Corticosteroids class 3 and 4 were the most effective for localized Vitiligo[35]. Topical potent and ultrapotent corticosteroids should be limited to 2–4 months to avoid local side effects (atrophy, telangiectasia, striae) and percutaneous absorbtion resulting chronic adrenal insufficiency[34].

Systemic corticosteroids:

Systemic corticosteroids may arrest the progression of vitiligo and lead to repigmentation by immunosuppression[36]. As clinical improvement is experienced by patients who are receiving oral corticosteroid treatment for actively spreading Vitiligo, a reduction in complement – mediated cytotoxicity by autoantibodies to melanocytes, and a reduction of antibody titre to surface antigens of melanocytes are noted in their serum samples.

Immunomodulators

Initial observations suggested that tacrolimus inhibits T-cell activation by down-regulating the transcription of genes encoding proinflammatory

cytokines. It offers the advantage of prolonged treatment without the adverse effects seen in the long-term use of corticosteroids.[34][36]

Lasers:

The 308-nm excimer laser produces faster repigmentation rates than any other medical method so far reported[37]. The 308-nm excimer laser demonstrated its efficacy and good tolerance for localized vitiligo. Repigmentation seems to be faster than with NB UVB, except in extremities and bony prominences. Since no data for skin cancer risk are available, caution is adviced.

Alternate and adjuvant therapies:

Vitamin D-3

Vitamin D-3 analogues calcipotriol and taclacitol have been used topically in vitiligo, where modulation of the local immune response on specific T cell activation occurs; they also influence melanocyte maturation and differentiation and up-regulate melanogenesis through pathways activated by specific ligand receptors, such as ET receptor and c-kit[38].

Depigmentation

Some selected patients with vitiligo universalis may benefit from depigmentation of unsightly residual pigmented patches on facial and exposed areas. Depigmentation may be achieved with 20% monobenzone

which is first applied with a patch test for 48 h to detect hypersensitivity; then, twice daily applications are followed by depigmentation within the next 6–12 months[39].

Psychological support and camouflage

If all treatments have failed; the patient does not wish to undergo treatment; or while treatment is ongoing, cosmetic cover-ups can be very useful. A recent study investigated quality of life in vitiligo patients and the effect of using camouflage. Using camouflage, particularly for the face, head and neck improved the patients' quality of life.

Surgical therapy

Until 1983, most articles referred to vitiligo as a condition treated exclusively with medical therapy. Early work with thin dermoepidermal grafts suggested that surgery had a place for vitiligo depigmentation[40]. Later on, the value of grafts for vitiligo therapy was confirmed.

Essentially five basic methods for melanocyte transplantation have been described:

1) non-cultured epidermal suspensions
2) thin dermo-epidermal grafts
3) suction epidermal grafting
4) minigrafting and punch grafting

5) in-vitro cultured epidermis with melanocytes or pure melanocyte suspensions.

All methods provide good to excellent results and the most important factors for success are patient selection and surgeon's expertise[34].

PHOTOTHERAPY AND PHOTOCHEMOTHERAPY

Historical background

The ancient Egyptians were the first to recognize the beneficial effect of sunlight on humans. Herodot in 525 BC correlated the strength of the human skull to the degree of sun exposure. The ancient Greeks (Hippocrates 460- 375 B.C., Obrasius of Pergamon 325-403 A.D.) used sunlight for a variety of illnesses including edema and diseases of the abdomen and kidneys.

Thereafter followed the dark period of phototherapy. In the Middle Ages, where pale skin was taken as a sign of beauty and wealth, phototherapy floundered. Newton in 1672 discovered the spectrum of visible light. Ultraviolet light was discovered in the early 1700s.

In 1895, modern phototherapy began when Niels Finsen, the father of modern ultraviolet therapy, used a carbon arc source to treat lupus vulgaris. He was awarded the Nobel prize in 1903.

In 1923, Goeckerman introduced his regime (artificial broadband UVB + coal tar) for psoriasis. In 1953 Ingram introduced his regime

combining artificial broadband UVB and dithranol. Subsequently, it was found that UVB on its own was also efficacious in dermatological therapy. Van Weelden in 1984 demonstrated the clinical efficacy of narrowband UVB. Since then, it has been proved to be more effective than broadband UVB in various skin disorders and is increasingly used in various parts of the world[41].

The history of photochemotherapy dates back to ancient times. As far back as 2000 B.C., the Indians and Egyptians used the pigment-stimulating properties of the psoralen-containing Bavachee plant (Psoralea corylifolia) and Ammi majus respectively for the treatment of Vitiligo. Only 3 millennium later in 1947 Fahmy, an Egyptian pharmacologist, isolated psoralen compounds from Ammi majus. The 1960s and 70s were an era where the basic pharmacology of the psoralens was studied. In 1974, Parish successfully introduced a treatment combining 8-methoxypsoralen and UVA called PUVA using newly developed Henselar high intensity artificial UVA light[42][43].

PHOTOBIOLOGY

Interaction between UV radiation and the skin.

UV radiation that reaches the skin is either reflected or absorbed by structures of the skin. While UVC (<280 nm) is mostly absorbed in the stratum corneum, UVA (320–400 nm) shows deeper penetration than UVB

(280-320nm). Thus UVB is mainly absorbed by epidermal components, including keratinocytes, melanin and Langerhans cells. Biological effects of UV radiation are generated through interaction with absorbing molecules called chromophores..Ultimately, the interaction of UV with chromophores can lead to a multitude of effects such as induction of oxidative stress and activation of transcription factors, as well as induction of damage to the cell membrane and DNA mutations[44].

PUVA

Ultraviolet-A (UVA) is the name given to the waveband of electromagnetic radiation ranging from 320-400nm. UVA combined with a psoralen photosensitizing agent (8-methoxypsoralen or 5-methoxypsoralen) is known as PUVA or photochemotherapy.

PUVA units are full body cabinets containing 6 feet 100W fluorescent low-pressure mercury bulbs., UVA lamps (TL100/209R) have black markings (e.g. FS72T12BLHO). Most units have 24 or 36 or 48 bulbs, and may be the same cabinet as BB-UVB and rarely NB-UVB bulbs. Hand & foot units contain 2 feet bulbs.

Modern units have integrated dosimetry and the time to deliver the correct dose is automatically calculated. For older units, irradiance is checked manually prior to treatment using a specific UVA dosimeter and the treatment time for a specific dose determined according to a spreadsheet [45].

Psoralens

Psoralens are chemical compounds derived from certain plants such as ‘Ammimajus’ found in Egypt and Indian plant Bavachee which is also called as Psoralea corylifolia. Psoralen has been found in more than 30 plants such as lime, lemon, bergamot, parsley, celery, fig and cloves[46]. The medical use of these plants in the treatment of vitiligo by the ancient Egyptians dates back to as early as 1500 B.C. and by the Indians to 1400 B.C.

Psoralen and many of its derivatives are naturally occurring tricyclic furocoumarins. The derivative most widely used in photochemotherapy is 8methoxypsoralen (8MOP, methoxsalen, xanthotoxin) which is principally of plant origin but it is available as a synthetic drug. The drug 4, 5, 8-trimethyl psoralen (TMP, trioxsalen) is a synthetic compound which is less phototoxic after oral administration and is primarily used for the treatment of vitiligo. Newer psoralens under research are 5-methoxypsoralen (Bergapten, 3-carbethoxypsoralen and angelicin). The photobiological activity of angelicin is low. The introduction of one or more methyl groups results in the increased photo binding capacity of angelicin towards DNA. These various methyl derivatives of angelicin are called the new angelicins. 4,, 6-methyl angelicin is the most promising of the new angelicins[47].

Pharmacology

When taken by mouth, methoxsalen (8-MOP) is absorbed from the gastrointestinal tract. Increased photosensitivity is present 1 hour after the dose, reaches a peak at about 2 hours and disappears after about 8 hours. The absorption of methoxsalen and hence clinical response may be altered by concomitant food ingestion as well as by differences in drug formulations. A liquid preparation in soft gelatin capsules or a microenema gave higher serum concentration more rapidly than did crystalline methoxsalen in tablets or capsules. Methoxsalen has high but variable intrinsic metabolic clearance and is almost completely metabolised. Individuals with a high clearance and low maximum serum concentration usually show reduced sensitivity to PUVA. These patients i.e. those not responding to usual dose may respond to higher doses of psoralens or to the administration of the drug by other routes such as bath water delivery. After oral administration the drugs are metabolised in the liver by hydroxylation and glucuronide formation and over 90% is excreted in the urine within 12 hours. Psoralen appears to be distributed to all tissues after oral administration and there is no risk of accumulation in any organ in patients with normal liver and kidney function.

When applied locally 8-MOP rapidly penetrates the skin and can be detected in the urine after 4 hours. The plasma levels of 8-MOP in patients receiving total body topical 8-MOP are comparable to those found during

oral 8-MOP ingestion. The plasma concentration of TMP after bath treatment is only approximately 1% of the plasma after oral ingestion.

Mechanism of action

The exact mechanism by which psoralens produce cutaneous photosensitivity reactions is not precisely known. Mode of action of psoralens does not occur at one level, but at several levels simultaneously including cellular DNA, RNA, proteins, mitochondria, cell membrane lipids etc. In the normal skin or in the skin of psoriatic patients, psoralen induced skin photosensitization involves two distinct types of reactions occurring independently of each other and concurrently when psoralen treated skin is exposed to 320 - 400nm radiation.

1. Type I is an anoxic reaction not requiring oxygen and the site of cellular damage is primarily in DNA of cell nuclei.
2. Type II is a sensitized reaction dependent on oxygen and involves the formation of oxygen reactive species and free radicals.

In these 2 modes of reactions, the reactive form of psoralen is in its triplet state. The major photochemical reaction of psoralen contributing to the cellular damage is undoubtedly the formation of monofunctional and bifunctional adducts of psoralen with pyrimidine bases in DNA . The formation of monofunctional and bifunctional photo adducts in DNA results in immediate inhibition of DNA synthesis. It is also possible that PUVA may

affect specific cells such as lymphocytes or polymorphonuclear leucocytes. A decrease in the percentage of circulating T-lymphocytes following PUVA treatment has been reported.

The mechanism by which PUVA induces repigmentation in vitiligo remains unclear although the following ways have been speculated.

1. By increasing the number of functional melanocytes as a result of mitosis or by activation of dormant melanocytes in the epidermis and appendages.
2. By inducing hypertrophy of melanocytes and an increased arborization of their dendrites.
3. By augmenting the development and melanization of melanosomes and increasing the transfer of melanosomes to keratinocytes.
4. By stimulation of tyrosinase activity
5. By enhancing the migration of activated melanocytes from skin appendages
6. By generating a suppressor cell population which suppresses the stimulus for melanocyte destruction during therapy[48]

Indications of PUVA

The indications are: (1) Psoriasis (2) vitiligo (3) cutaneous T-cell lymphoma (4) atopic dermatitis (5) lichen planus (6) urticaria pigmentosa (7) preventive treatment for photodermatoses like (a) polymorphic light eruption

(b) solar urticaria (c) chronic actinic dermatosis (d) persistent light reaction (e) hydroa vacciniforme and (8) miscellaneous conditions such as acute and chronic pityriasis lichenoides, lymphomatoid papulosis, pityriasis rubra pilaris and alopecia areata.[48]

Methods of treatment

For oral 8-MOP, 0.4 to 0.6 mg/kg body weight is usually effective, although some may need more, and others less. For 5-MOP, double this dose is necessary (1-1.2 mg/kg body weight). Poor response to PUVA can be due to inadequate absorption of the drug or a delayed peak levels of psoralen in the skin.

The minimal phototoxic dose (MPD) is typically measured as follows.

1. 0.5 mg/kg of methoxsalen is ingested 2 hours prior to exposure.
2. A template with four or five 1 to 2-cm squares is applied to a non-sun exposed area (often volar surface of forearm or buttocks). The Diffey device is convenient for this purpose. The templates block the radiation by nil, a half, three-quarters and seven-eighths. Surrounding skin is protected from exposure. The squares are exposed to a geometric series of increasing doses of UVA according to estimated skin type. (e.g. 1, 2, 4, 8 J/cm2).
3. Test sites are outlined with a skin marker so that they can be identified.

4. The response is measured 72-96 hours later. The MPD is the lowest dose of UVA radiation that produces pink erythema with distinct borders.
5. The test may be repeated using a different range of test doses if either all or none of the test sites have erythema.

Dose regimen for PUVA

To establish the appropriate starting dose of UVA,MPD is determined and the initial dose is fixed at 70% MPD. Or the dose is selected according to estimated skin type as shown in the table If case of obese patients, skin is assumed one type less as irradiance will be greater as the patient's body is closer to the bulbs. Dose has to be slowly increased with weekly increments. Patients with Skin type 1 & 2 were treated twice weekly to reduce chance of erythema.

Skin type	Initial dose (J/cm^2)	Increments	Maximum dose (J/cm^2)
Skin type 1	1	30 % each week	5
Skin type 2	2	30% each week	8
Skin type 3	3	30% each treatment	20
Skin type 4	4	30% each treatment	20
Skin type 5	5	30% each treatment	20
Skin type 6	6	30% each treatment	20

The development of any phototoxic erythema precludes further dose increments. It may be very difficult or impossible to treat skin phototype 1 patients with PUVA. The patient should be examined prior to each treatment. Erythema may be localised or generalised. Localised erythema can be protected allowing incremental exposures to the rest of the body, as scheduled, but generalised erythema should result in changes to the schedule. No erythema - dose is according to schedule. Faint erythema (pink) or mild itch - dose is held at previous level. Definite or tender erythema(pink) or significant itch - treatment is withhold until erythema resolved [45].

US protocol

The first treatment exposure dose is based on the skin typing and the patients are treated either twice or thrice a week. Dose increments range from 0.5 - 1.5 J/cm2 depending on erythema production and therapeutic response[47].

European protocol

The first treatment is administered after determination of the individual's minimum phototoxic dose (MPD) and the initial UVA dose is 70% of the patients MPD. Four treatments are given per week. Two treatments are given on consecutive days followed by a rest on day 3 after which treatment is resumed for 2 days. Increments of dose are performed

only after the first four treatments if no more than a pink erythema has developed and range from 0.5 to 2 J/cm^2 depending on the patient's MPD ability to develop pigmentation[47].

Manipal protocol:

The usual starting dose is 4 - 6J/cm^2. Dosage increments of 0.5 J/cm^2 are done each time till a maximum of 18 J/cm^2 is reached. Treatment is given thrice or four times a week[47].

Precautions to be taken during PUVA therapy

Because of the greater likelihood of photoageing and carcinogenesis, PUVA should not be used in children. It should only be used in patients who are able to comprehend and comply with instructions. Psoralen requires hepatic metabolism and renal excretion therefore should be used with great care in those with hepatic or renal disease. It is not teratogenic, but like other medications should be avoided in pregnancy if possible. It is excreted in breast milk, so breast-feeding mothers should not receive PUVA. Carbamazepine, phenytoin and phenobarbitone reduce the level of methoxsalen. Systemic methoxsalen inhibits liver enzymes so that it may significantly increase serum levels of concomitant caffeine or theophylline[45].

Adverse side effect of PUVA therapy

Acute side effect

- Anorexia
- nausea
- headache
- dizziness
- Acute phototoxicity: tender erythema &/or deep pruritus for several weeks or longer
- Ocular toxicity: photokeratitis causing grittiness, pain, photophobia, tearing & blepharospasm
- Polymorphic light eruption
- Irritable erythematous papules on skin that is not usually sun-exposed
- Herpes simplex reactivation.....
- Koebnerisation from phototoxicity
- Rarely: asthma, hepatitis, drug fever, rash, photo-onycholysis, ankle oedema, hypertrichosis

Long-term side effect

- Photo-ageing: Wrinkling, PUVA freckling, xerosis, telangiectasia, elastosis, white macules, skin atrophy, cataracts
- Solar keratoses, squamous cell carcinoma (SCC), basal cell carcinoma (BCC) & melanoma. Risk of SCC is greater if >200 treatments, especially for skin type 1 & 2 and if there are other predisposing

factors such as excessive sun exposure. The risk of genital skin cancer is high so genitalia should always be covered during PUVA therapy[45].

UVB PHOTOTHERAPY

Phototherapy with ultraviolet (UV) radiation of wavelengths between 280 and 320 nm (UVB) is a safe and effective treatment for a variety of diseases. In addition to standard broadband UVB (BBUVB), narrowband phototherapy with fluorescent bulbs emitting monochromatic UV around 311 nm (NBUVB) has become an important treatment for diseases such as psoriasis, atopic dermatitis and vitiligo.[49]

Mechanism of action

UV radiation alters immunological function and UVB can increase the production of pro-inflammatory substances like prostaglandins (PG) or tumour necrosis factor (TNF), as well as the production of anti-inflammatory factors like interleukin (IL)-10, alpha-melanocyte stimulating hormone (MSH) and PGE2[50]

UVB down-regulates the expression of intercellular adhesion molecule (ICAM)-1, reduction of the density and function of Langerhans cells in the skin and their migration to the draining lymph nodes is more pronounced with BBUVB than with NBUVB. Infiltrating epidermal T cells as well as mast cells are susceptible to UVB-induced apoptosis. NBUVB

appears to have a more immunosuppressive effect than BBUVB on natural killer cell activity, cytokine responses and lymphoproliferative responses of peripheral blood mononuclear cells and photo-isomerization of trans- to cis-urocanic acid is more effective with NBUVB than with BBUVB with urocanic acid photoconversion being mainly induced by wavelengths between 310 and 340 nm.[51]

NBUVB suppresses the production of interferon (INF) - α, IL-2 and IL-12 and increases that of IL-4 and IL-10, which together could account for a shift of the immune response in the direction of T-helper (Th)2-like responses . The shift from an IFN-α-dominatedTh1 to an IL-4 dominated Th2 response appears t o be one of the major factors determining the therapeutic efficacy of NBUVB phototherapy.[52]

NB UVB may exect its effects in vitiligo in a two – step process. Both steps may occur simultaneously, that first being the stabilization of the depigmenting process and the second, the stimulation of residual follicular melanocytes. The well documented inmmunomodulating effects of UV radiation can explain stabilization of local and systemic abnormal immune responses. Its also likely that NB UVB similar to PUVA therapy. Stimulates the dopa – negative, amelanotic melanocytes in the outer hair root sheaths, which are activated to proliferate, produce melanin and migrate out ward to adjacent depigmented skin resulting in perifollicular repigmentation.

INDICATIONS FOR NARROWBAND UVB

Phototherapy with NBUVB has been reported to be effective and safe for the treatment of psoriasis, atopic dermatitis and vitiligo. Various other skin diseases can be treated successfully with NBUVB phototherapy, like parapsoriasis, initial mycosis fungoides, graft-versushost disease and pruritus, as well as acquired perforating dermatosis, lichen planus, lichen simplex chronicus, lymphomatoid papulosis, generalized granuloma anulare nummular dermatitis, pityriasis lichenoides chronica, pityriasis rosea, pityriasis rubra pilaris, pruritic folliculitis of pregnancy, seborrhoeic dermatitis, Schnitzler's syndrome and Sneddon-Wilkinson disease.[49]

ADVERSE EFFECTS OF NB-UVB

Early side effects

Early side effects of NBUVB include erythema and dryness of the skin. The maximum erythema occurs 8–24 h after irradiation. As patients over 70 years show a prolonged NBUVB-induced erythema, a more cautious approach to dose increment is recommended in the elderly.[54]

Late side effects

Chronic exposure to UV radiation induces premature ageing (photo ageing) of the skin, showing typical clinical signs of leathery appearance, wrinkling, reduced recoil capacity and increased fragility of the skin. [55]

VITILIGO TREATMENT RESPONSE ASSESSMENT

Many vitiligo treatments have typically been analyzed using nominal binary scales in which the proportion of treated patients who either do or do not achieve a specified degree of repigmentation is reported and compared by nonparametric statistical approaches. The degree of repigmentation that defines success has often been set somewhat arbitrarily at 50% to 75% repigmentation based largely on the global impression of the overall response. There is currently no validated quantitative scale that allows vitiligo to be characterized parametrically.

The primary advantage of using quantitative scales for evaluating vitiligo is that they provide direct estimates of the expected quantitative responses that patients might expect to achieve. In contrast, nominal and nonparametric methods can only estimate the proportion of patients who achieve a certain arbitrarily set level of response. Quantitative methods provide data that are generally more intuitive and meaningful to patients and physicians, while at the same time being more sensitive for detecting significant subtle treatment effects.[56] VASI scoring is one such quantitative method however which is not routinely perform.

Vitiligo treatment response assessment scales followed by different authors are summarised in the table below.

Treatment type	Percent clearance and classification				Authors
	0%-25%	26%-50%	51%-75%	76%-100%	
Medical					
	Poor	Fair	Good	Excellent	Hann et al[6]
	Poor	Moderate	Good	Excellent	Yalcin et al[7]
	Slight	Moderate	Marked	Excellent	Radakovic-Fijan et al[1]
	Minimal	Mild	Moderate	Excellent	Grimes et al[2]
Narrowband ultraviolet B radiation					
	<25% Response	Between 26%-75% response		>75% response	Njoo et al[8]
		Poor response		Best response	Scherschun et al[3]
Surgical					
	Grade 1 <10% as no repigmentation	Grade 2 >10%-<95% as partial repigmentation		Grade 3 >95% as complete repigmentation	Spencer et al[4] Kim et al[5]

Previous studies comparing PUVA and NBUVB therapy in Vitiligo

In their meta analysis Njoo *et al* concluded that the difference between mean success rate of NB – UVB and PUVA are not statistically significant although the former was comparatively more effective. [57]

In their randomized double blind trial , Sami Sasi Yones et al found that 64% of patient in the NB UVB group showed greater than 50 % improvement compared to 36% patient only in PUVA group.[58]

In the open and non -observer blinded study comparing the systemic PUVA and NB UVB in the treatment of vitiligo (A Bhatnager et al) The mean repigmentation achieved in NB UVB group 52 .24% and PUVA group 44.7% which was statistically not significant.[59] How ever after excluding the resistant sites that is hands and feet The mean repigmentation achieved in NB UVB group 67.57% and PUVA group 54.2% which was statistically significant.

The retrospective study by Parsad et al, PGI Chandigarh 23.6% showed marked to complete improvement and 36.8% moderate improvement in the PUVA treated group whereas in the NB – UVB group 41.9% showed marked to complete repigmention 32.2% showed moderate improvement.[60]

MATERIALS AND METHODS

This randomised open prospective clinical study was conducted on forty Vitiligo vulgaris patients who attended outpatient clinic of Dermatology department at Tirunelveli medical college hospital, Tirunelveli over the period of 15 months from April 2009 to June 2010. Approval was obtained from the institutional ethical committee prior to the conduct of this study.

PATIENT SELECTION

Inclusion criteria:

a. Age 18 to 65 years
b. Body surface area involvement greater than 10%
c. Stable Vitiligo (Stable for more than one year)

Exclusion criteria:

a. Age less than18 years and more than 65 years
b. Body surface area involvement lesser than 10%
c. H/o Photosensitivity and Photo mediated disorders
d. H/o administration of drugs causing photosensitization
e. H/o skin malignancy, renal and hepatic diseases
f. Pregnancy and Lactation
g. Active Vitiligo
h. Patient on any treatment for Vitiligo within previous 6 months

The name, age, sex, address, outpatient number were noted. Following detailed clinical history was taken.

1. Time of onset of Vitiligo
2. Course of the disease-stability and rate of progression
3. Potential precipitating events including emotional stress and cutaneous trauma
4. History of photosensitivity and drug causing photosensitivity
5. History of any treatment(Systemic, topical)
6. Any history of suggestive of Diabetes Mellitus , Hypertension, Thyroid disease, Anaemia and other autoimmune diseases
7. Family history of Vitiligo
8. History of any psychological impact by the Vitiligo

All patients were examined under good light. Detailed dermatological examination including size, shape, number, color and distribution of lesions was done. Pattern of Vitiligo and mucosal involvements were taken into account. Presence of leucotrichia in the patch was also noted.

Estimation of percentage of body surface area with Vitiligo was carried out by using rule of 9 (Wallace), 9% for head and neck (head 7%, neck 2%), 9% for each upper limb (arm 4%, forearm 3% hand 2%) 9% for the front of each lower limb (Thigh 5%, leg 2.5%, foot1.5 %) and 9% for the back of each lower limb (Thigh 5%, leg 2.5%, foot1.5 %). 9% for the front

of chest, 9% for the front of the abdomen, 9% for the upper back, 9% for the lower back and 1% for the external genitalia.

Palm size is taken as about 1% of body surface area for measuring small area of involvement. Any skin lesions suggestive of autoimmune disorders like Autoimmune thyroiditis, Diabetes mellitus, pernicious anaemia, Addison's disease if present were noted.

Laboratory investigations like routine blood examination (Hb, TC, DC & ESR), urine analysis, blood sugar, blood urea and serum creatinine, liver function tests, thyroid function test were done. ophthalmic examination was done to rule out cataract and retinal pathology

Initial photographs were taken using canon digital camera before commencement of treatment, completion of every sixteen treatment sessions and at the end of the treatment.

Patients were randomly allocated to receive either PUVA or narrow band UVB by means of a sequentially numbered list

Treatment schedule, precaution to be taken during and after treatment, expected response, total duration of treatment and common side effects were explained to the patient. Informed consent was obtained from the patients before starting treatment.

Phototherapy unit:

Full body phototherapy chamber containing 6 feet, 100W fluorescent UVA and NBUVB lamps total of 36 bulbs. This chamber has integrated dosimetry and the time to deliver the correct dose is automatically calculated.

The following treatment methodology and assessment of response were adapted during the study between the two groups.

TREATMENT SCHEDULE

A. PUVA groups

Patients were instructed to ingest trimethyl Psoralen 25 mg tablet empty stomach two hours before UV exposure. Standard initial dose of 5 Joules/cm ^{2} was given to all patients. Therapy was administered twice per week on Tuesdays and Fridays. Irradiation dose was increased by 0.5 Joules /cm ^{2} per week. During each treatment session, patients were instructed to shield their genitals and use photo protective goggles. Barring these protected areas whole body irradiation was performed. If lesion was present on the eyelids, patients were asked to close the eyes during treatment without wearing goggles. Patients were advised to apply sunscreen on exposed areas after treatment and to avoid excessive sun exposure.

B. Narrow band UVB

Standard initial dose of 250mJ/cm ^{2} was given to all patients. Therapy was administered twice per week on Tuesdays and Fridays. Irradiation dose was increased by 50 mJ /cm ^{2} per week. During each treatment session patients were instructed to shield their genitals and use photo protective goggles. Barring these protected areas whole body irradiation was performed.

Optimal constant dose

The development of any phototoxic erythema precludes further dose increments. Erythema may be localized or generalized. If localized erythema present that parts were covered and allowing incremental exposures to the rest of the body, as scheduled. But when generalized erythema occurred, then the schedule was stopped until the resolution of erythema. Once erythema resolved, the optimal constant dose was held at the previous dose.

Assessment of therapy

Fortnightly repigmentation assessment including follicular pigmentation, shrinkage of the lesion and color of the lesion (diffuse pigmentation) was noted and recorded.

The affected areas Photographs were taken on completion of every 16 sessions. Comparison was made with the base line photograph to determine the percentage of improvement in body surface area of Vitiligo.

Repigmentation was graded in each topographical area as follows

- Grade 0 = 0% (No response)
- Grade 1 = 1-25 % (Mild)
- Grade 2 = 26-50% (Moderate)
- Grade 3 = 51-75% (Good)
- Grade 4= 76-99% (Very good)
- Grade 5 = 100% (Excellent)

Mean repigmentation in individual patients were calculated by adding the extent of repigmentation achieved in each topographical area after therapy and then dividing the figure with the total number of tophographical areas bearing Vitiligo lesions. Mean repigmentation in the individual group was determined by adding the mean repigmentation of the individual patients divided by number of patients in each group.

Colour of repigmentation was graded subjectively as somewhat darker, somewhat lighter or the same as compared with a normally pigmented surrounding skin. Time taken for onset of repigmentation was noted. Any adverse effects during treatment were noted.

Psychological Assessment

The subjective satisfaction of the patient is assessed by asking the question “How do they feel about the treatment?” The patient were

instructed to give any one of the following response 1.Unsatisfied 2.Satisfactory 3.Good 4.Very good 5.Excellent

This question is asked at the end of every 16 treatment sessions, and the response is noted and recorded.

Termination of therapy

Treatment was stopped once 100% repigmentation was achieved or the 12 months period was completed whichever was earlier. Patient showing no response after 50 exposure was considered as a non responder and excluded from the study.

Results were analised by students propotion ‘t’ test and students unpaired ‘t’ test. The effectiveness of therapy between two groups were compared by students unpaired ‘t’ test. Colour match, psychological satisfaction, and side effects of therapy were compared by chi- square test. The above statistical procedure were performed by statistical package SPSS(13.0).

RESULTS

Out of the 20 patient enrolled for study in each group, only 15 patients completed the study. 5 patients in each group stopped due to various reasons within 3 months and so excluded from the study. In both groups there were no non responders after 50 treatment sessions.

PUVA GROUP:

1) Demographic profile

In PUVA group age of the patients ranges from 18-60. Mean age with Standard deviation (S.D) is 41.06±13.63. There are 4 males and 11 females. (Table 1&2)

The duration of disease ranges from 2 yrs to 15 years(yrs). Mean duration of Vitiligo with S.D is 4.53±2.19 yrs (Table:3). The body surface area affected by vitiligo ranges from 13% to 47%. Mean body surface area affected by vitiligo with S.D is 24.9±9.95 (Table:4). The duration of therapy ranges from 6 months to 8 months. The mean duration of therapy with S.D is 6.85±0.99 months.

2) Initial Repigmentation:

Time taken for initial repigmentation ranges from 4 to 12 weeks. The average time taken for initial repigmentation along with S.D is 6.93±2.8 weeks. (Table:5)

3) Mean grade of treatment response

Area wise mean grade of repigmentation after five months therapy is as follows, Face - 1.83, Neck - 1.8, Anterior trunk - 1.33, Posterior trunk - 1.5, Upper limb - 1.67, lower limb - 1.57, Hands - 1.07, feet - 1 and at the end of treatment as follows Face - 2.16, Neck - 2.6, Anterior trunk - 2.16, Posterior trunk - 2, Upper limb - 2.5, lower limb - 2.38, Hands - 1.28, feet - 1.18. (Table 6, 8)

At the end of 5 months of therapy 2 persons (13%) are in grade 1, 12 persons (80%) are in grade 2, 1 person (7%) is in grade 3. At the end of the treatment 1 person (7%) is in grade 1, 7 persons (46.5%) are in grade 2, 7 persons (46.5%) are in grade 3. (Table : 10)

The mean grade of treatment response at 5 months is 1.45 whereas. Mean grade of treatment response at the end of the treatment is 2.01 (Table : 13)

After excluding the resistant sites i.e hands and feet, the mean grade of treatment response at 5 months is 1.61 and at the end of the treatment is 2.3 (Table : 14).

COLOUR MATCH:

Only in 7 patients the colour of repigmentation is same as that of surrounding skin, whereas in 8 patients the repigmentation was darker than the surrounding skin. (Table: 15)

PSYCOLOGICAL SATISFACTION:

Out of the 15 patients 8 patients (53%) has good satisfaction, 6 patients has only moderate satisfaction. One patient was not satisfied with the treatment.

SIDE EFFECTS:

6 patients (40%) experienced side effects. Nausea and vomiting occured in 2 patients, itching and burning sensation were noted in 4 patients.

NB-UVB GROUP:

1) Demographic profile

In NB-UVB group age of the patient ranges from 18-65 yrs. Mean age with S.D(S.D) is 34.±12.80. There are 5 males and 10 females. (Table: 1,2)

The duration of disease ranges from 2 yrs to 10 yrs. Mean duration of Vitiligo with S.D is 4.96±3.67. (Table:3) The body surface area affected by vitiligo ranges from 13% to 48%. Mean body surface area affected by vitiligo with S.D is 23.83±11 (Table:4). The duration of therapy ranges from 6 months to 10 months. The mean duration of therapy with S.D is 7.26±1.22. (Table 1 & 2)

2) Initial Repigmentation:

Time taken for initial repigmentation ranges from 4 to 12 weeks. The average time taken for initial repigmentation in NB-UBV groups is 6.6 ±2.6 weeks (Table:5)

3) Mean grade treatment response

Area wise mean grade of repigmentation after five months of therapy is as follows Face - 2, Neck - 1.67, Anterior trunk - 2.36, Posterior trunk - 2.2, Upper limb - 2, lower limb - 1.84, Hands - 1.2, feet - 1.07, at the end of treatment as follows Face - 3, Neck - 2.67, Anterior trunk - 3.18, Posterior trunk - 3, Upper limb - 2.9, lower limb - 2.69, Hands - 1.53, feet - 1.4. (Tables: 7,9)

At the end of 5 months of therapy 4 persons (27%) are in grade 1, 9 persons (60%) are in grade 2, 3 persons (13%) are in grade 3. At the end of the treatment 1 person (7%) is in grade 1, 3 persons (20%) are in grade 2, 7 persons (46.5%) are in grade 3, 4 persons are in grade 4. (Table:10)

The mean grade of treatment response at 5 months is 1.71. Mean grade of treatment response at the end of the treatment is 2.5. (Table:13)

After excluding the resistant sites i.e hand and foot grade of treatment as follows. The mean grade of treatment response at 5 months is 2.01 Mean grade of treatment response at the end of the treatment is 2.9. (Table:14)

COLOUR MATCH:

Repigmentation occurred in Vitiligo patches after treatment was exactly same as that of surrounding skin in 13 patients. Only in 2 patients repigmentation is darker than surrounding skin that too only in the margins. (Table:15)

PSYCOLOGICAL SATISFACTION:

Out of the 15 patients one patient has excellent satisfaction, 9 patients has good satisfaction. 3 patients reveal only moderate satisfaction. One patient was not satisfied with the treatment

SIDE EFFECTS:

Out of 15 patient 5 patients developed side effects. Itching is the common side effect which was noticed in 4 patients. One patient developed blisters in lip on first day of therapy which cleared within 2 days.

Table : 1. Demographics and patient parameters

	PUVA	NB-UVB
Number of patients	15	15
Age in years (Mean ±SD)	41.06±13.63	34±12.80
Range in years	18-65	18-60
Sex (Male/Female)	4/11	5/10
Duration of the Disease in years (Mean ±SD)	4.53±2.19	4.96±3.67
Range in years	2-10	2-15
Body surface area in percentage (Mean ±SD)	24.9±9.95	23.83±11.96
Range in percentage	13-48	11-47
Duration of therapy in Months (Mean±SD)	6.85±0.99	7.26±1.22
Range (Months)	6-8	6-10

Table: 2. Age and sex wise distribution

Age Group (Years)	PUVA		NB-UVB	
	Male (%)	Female (%)	Male (%)	Female (%)
18-30	1(6.6%)	3(20%)	2(13%)	4(26.6%)
31-40	1 (6.6%)	1 (6.6%)	0 (0%)	3 (20%)
41-50	1(6.6%)	2 (13%)	2(13%)	3 (20%)
51-60	2(13%)	4(26.6%)	0(0%)	1 (6.6%)
TOTAL	5(33%)	10 (67%)	4(26.6%)	11(73.4%)

Table :3. Comparison of duration of disease in years between two groups

Duration (years)	PUVA		NBUVB		Mean±S.D		't' Test	Significance
	No of patients	%	No of patients	%	PUVA	NBUVB		
1-5	9	60.0	8	53.4	4.53 ± 2.19	4.96 ± 3.67	0.392	P>0.05
6-10	5	33.3	5	33.3				
11-15	1	6.7	2	13.3				
Total	15	100.0	15	100.0				

Table :4. Comparison of body surface area affected by vitiligo between both groups

Surface area (percentage)	PUVA		NBUVB		Mean±S.D		't' test	significance
	No of patients	%	No of patients	%	PUVA	NBUVB		
10-20	4	26.7	7	46.7	24.8 ± 10.0	23.8 ± 12.0	0.241	P>0.05
20-30	8	53.3	2	13.3				
30-40	2	13.3	4	26.7				
40-50	1	6.7	2	13.3				
TOTAL	15	100.0	15	100.0				

Table :5. Comparison of time taken for initial repigmentation between both groups

Duration (weeks)	PUVA		NB-UVB		Mean ± S.D		Chi-square value	d.f	Significance
	No of patients	%	No of patients	%	PUVA	NBUVB			
4 - 7	8	53.4	11	73.4	6.9 ±2.6	6.6 ±2.6	5.400	1	P>0.05
8 – 11	5	33.3	2	13.3					
12 - 15	2	13.3	2	13.3					

Table: 6. Treatment Response for PUVA Therapy at 5 Months

(Response in Grades*)

S No	Name	Face	Neck	Ant Trunk	Post trunk	UL	LL	Hands	Feet	Average grade of response
1	Ramaiah	-	2	1	-	2	2	1	1	1.5
2	Mohamed Hasan	2	-	-	-	2	2	1	1	1.6
3	Elizabeth	-	-	1	-	2	2	-	-	1.67
4	Pakiathai	2	-	-	-	-	2	1	1	1.5
5	Hussain	2	-	2	-	-	2	1	1	1.6
6	Parvathi	1	-	1	1	1	1	1	1	1
7	Lakshmi	1	-	-	-	1	1	1	1	1
8	Panchatcharam	2	2	-	-	2	1	1	1	1.5
9	Sundar Rajan	2	-	-	-	2	1	1	1	1.4
10	Muthu Lekshmi	2	-	-	-	1	1	1	-	1.25
11	Princy	2	-	2	2	3	3	2	1	2.14
12	Regina Banu	2	1	1	-	-	1	1	1	1.17
13	Sundari	2	-	-	-	2	2	1		1.75
14	Subathra Devi	2	2	-	-	1	-	1	-	1.5
15	Prema	-	2	-	-	1	1	1	1	1.2
	Average Pigmentation	1.83	1.8	1.33	1.5	1.67	1.57	1.07	1	1.45

Grade : 0 = 0 % (No Response)
Grade : 1 = 1-25% (Mild)
Grade : 2 = 26-50% (Moderate)
Grade : 3 = 51-75% (Good)
Grade : 4 = 76-99% (Very Good)
Grade : 5 = 100% (Excellent)

Table:7. Treatment Response for NB-UVB Therapy at 5 Months

(Repigmentation in Grades*)

S No	Name	Face	Neck	Ant Trunk	Post Trunk	UL	LL	Hands	Feet	Average grade of response
1	Arunachalam	2	-	3	2	3	2	1	1	2
2	Arumugam	2	-	2	-	-	-	1	1	1.5
3	Angela	2	-	-	-	-	3	1	1	1.75
4	Subbulaksmi	1	-	-	-	-	1	1	1	1
5	Gayathridevi	2	-	2	2	2	2	2	1	1.85
6	Kaliraj	1	1	1	1	1	1	1	1	1
7	Sarathu	-	-	3	3	3	-	2	2	3.2
8	Ramalingam	2	2	2	2	2	2	1	1	1.75
9	Gomathi	1	1	-	-	-	1	1	1	1
10	Gururajan	3	2	3	3	2	2	2	1	2.25
11	Sujatha	2	2	1	2	2	2	1	1	1.62
12	Manjula	-	-	-	-	1	1	1	1	1
13	Rajashree	-	-	3	3	2	3	1	1	2.17
14	Daisy	3	2	2	2	2	2	1	1	1.87
15	Mary Merceline	3	-	2	2	-	2	1	1	1.83
	Average Pigmentation	2	1.67	2.36	2.2	2	1.84	1.2	1.07	1.71

Grade : 0 = 0 % (No Response)
Grade : 1 = 1-25% (Mild)
Grade : 2 = 26-50% (Moderate)
Grade : 3 = 51-75% (Good)
Grade : 4 = 76-99% (Very Good)
Grade : 5 = 100% (Excellent)

Table:8. Treatment Response for PUVA Therapy at the end of the treatment

(Response in Grades*)

S No	Name	Face	Neck	Ant Trunk	Post trunk	UL	LL	Hands	Feet	
1	Ramaiah	-	3	2	-	3	3	1	1	2.16
2	Mohamed Hasan	2	-	-	-	3	3	1	1	2
3	Elizabeth	-	-	2	-	3	2	-	-	2.3
4	Pakiathai	3	-	-	-	-	3	1	1	2
5	Hussain	2	-	3	-	-	3	2	2	2.4
6	Parvathi	1	-	1	1	1	1	1	1	1
7	Lekshmi	1	-	-	-	2	2	1	1	1.4
8	Panchatcharam	2	3	-	-	3	2	1	1	2
9	Sundar Rajan	3	-	-	-	3	2	1	1	2
10	Muthu Lekshmi	2	-	-	-	2	2	2	-	2
11	Princy	3	-	3	3	4	4	2	1	2.85
12	Regina Banu	2	2	2	-	-	2	1	2	1.83
13	Sundari	3	-	-	-	3	3	2	2	2.6
14	Subathra Devi	2	3	-	-	2	-	2	-	2.25
15	Prema	-	2	-	-	2	1	1	1	1.4
	Average Pigmentation	2.16	2.6	2.16	2	2.5	2.38	1.28	1.18	2.01

Grade : 0 = 0 % (No Response)
Grade : 1 = 1-25% (Mild)
Grade : 2 = 26-50% (Moderate)
Grade : 3 = 51-75% (Good)
Grade : 4 = 76-99% (Very Good)
Grade : 5 = 100% (Excellent)

Table:9. Treatment Response for NB-UVB Therapy at the end of treatment

(Response in Grades*)

S No	Name	Face	Neck	Ant Trunk	Post Trunk	UL	LL	Hands	Feet	
1	Arunachalam	5	-	5	3	4	3	1	1	3.1
2	Arumugam	2	-	3	-	-	-	2	2	2.25
3	Angela	4	-	-	-	-	3	2	2	2.75
4	Subbulaksmi	2	-	-	-	-	2	1	1	1.5
5	Gayathridevi	2	-	3	2	3	3	2	1	2.28
6	Kaliraj	1	1	1	1	1	1	1	1	1
7	Sarathi	-	-	4	4	4	-	3	3	3.6
8	Ramalingam	3	3	2	3	3	3	1	1	2.63
9	Gomathi	2	2	-	-	-	2	1	1	1.6
10	Gururajan	4	4	4	4	3	3	2	1	3.25
11	Sujatha	3	3	3	3	3	3	1	1	2.5
12	Manjula	-	-	-	-	2	2	1	1	1.5
13	Rajashree	-	-	4	4	3	4	2	2	3.2
14	Daisy	4	3	3	3	3	3	1	1	2.63
15	Mary Merceline	4	-	3	3	-	3	2	2	3
	Average Pigmentation	3	2.67	3.18	3	2.9	2.69	1.53	1.4	2.45

Grade : 0 = 0 % (No Response)
Grade : 1 = 1-25% (Mild)
Grade : 2 = 26-50% (Moderate)
Grade : 3 = 51-75% (Good)
Grade : 4 = 76-99% (Very Good)
Grade : 5 = 100% (Excellent)

Table :10. Grading of repigmentation obtained including Resistant sites

Grade	5 Months		At the End of the Treatment	
	PUVA	NB-UVB	PUVA	NB-UVB
	Number of patients (%)		Number of patients (%)	
0	0 (0%)	0 (0%)	0 (0%)	0 (0%)
1	2 (13%)	4 (27%)	1 (7%)	1 (7%)
2	12 (80%)	9 (60%)	7 (46.5%)	3 (20%)
3	1 (7%)	2 (13%)	7 (46.5%)	7 (46.5%)
4	0 (0%)	0 (0%)	0 (0%)	4 (26.5 %)
5	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Table : 11. Grading of repigmentation obtained excluding Resistant sites

Grade	5 Months		At the End of the Treatment	
	PUVA	NB-UVB	PUVA	NB-UVB
	Number of patients (%)		Number of patients (%)	
0	0 (0%)	0 (0%)	0 (0%)	0 (0%)
1	2 (13%)	4 (26.5%)	1(7%)	1 (7%)
2	12 (80%)	4 (26.5%)	4 (26%)	3 (20%)
3	1 (7%)	7 (47%)	9 (60%)	6 (40%)
4	0 (0%)	0 (0%)	1 (7%)	5 (33%)
5	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Table : 12. Topographical areawise repigmentation at the end of treatment

Topographical area	Mode of therapy	No of Patients						Total Number of Patients With involvement
		No Response 0 %	0-25%	26-50%	51-75%	76-99%	100%	
Face	PUVA	0	2	6	4	0	0	12
	NB-UVB	0	1	4	2	4	1	12
Neck	PUVA	0	0	2	3	0	0	5
	NB-UVB	0	1	1	3	1	0	6
Anterior trunk	PUVA	0	1	3	2	0	0	6
	NB-UVB	0	1	1	5	3	1	11
Posterior trunk	PUVA	0	1	0	1	0	0	2
	NB-UVB	0	1	1	5	3	0	10
Upper limbs	PUVA	0	1	4	6	1	0	12
	NB-UVB	0	1	1	6	2	0	10
Lower limbs	PUVA	0	2	6	5	1	0	13
	NB-UVB	0	1	3	8	1	0	13
Hands	PUVA	1	8	5	0	0	0	14
	NB-UVB	0	8	6	1	0	0	15
Feet	PUVA	1	8	3	0	0	0	12
	NB-UVB	0	10	4	1	0	0	15

Table :13. Comparison of mean grade of treatment response between PUVA and NB-UVB therapy including the resistant site

Period	PUVA		NB-UVB		Difference of mean	't' Test	d.f	significance
	Mean	S.D	Mean	S.D				
At 5th month	1.45	0.3	1.7	0.6	0.3	1.556	28	p>0.05
At the end of the treatment	2.01	0.4	2.5	0.8	0.4	2.086	28	P<0.05

Table : 14. Comparison of mean grade of treatment response of two group excluding resistant site (without hands and feet)

Period	PUVA		NB-UVB		Difference of mean	't' Test	d.f	significance
	Mean	S.D	Mean	S.D				
At 5th month	1.61	0.2	2.01	0.2	0.4		28	P>0.05
At the end of the treatment	2.3	0.6	2.9	0.9	0.6	2.185	28	P<0.05

Table :15. Comparison of Colour match between both groups

Colour match	PUVA		NB-UVB		Chisqure value	d.f	Significance
	Mean	S.D	Mean	S.D			
Darker	8	53.3	2	13.3	5.400	1	P<0.05
Same	7	47.7	13	86.7			
Total	15	100	15	100			

TABLE :16. Impact of duration of treatment on Repigmentation

Group	At 5TH Month		At the end		Improvement		't'	d.f	Significance
	MEAN	S.D	MEAN	S.D	MEAN	S.D			
PUVA	1.4	0.3	2.0	0.4	0.6	0.2	6.389	14	P<0.001
NBUVB	1.7	0.6	2.5	0.8	0.8	0.3	8.615	14	P<0.001

DISCUSSION

Psoralen with Ultra violet A therapy (PUVA) is a well established treatment for Vitiligo vulgaris. It is used in the present form since 1976. However puvasol therapy has been in use since 2500 years (yrs).[11]

In 1997, Narrow Band Ultra Violet B therapy (NBUVB) was introduced by westerhof *et al* for vitiligo vulgaris management. NBUVB has been found to be effective in vitiligo in various studies over the period.[61]

There are only few studies comparing the efficacy and safety of PUVA and NBUVB therapy in the treatment of Vitiligo[57&58&59&60], this is one such study.

Demographic and disease parameters:

In this study, in the PUVA group age of the patients ranges from 18-65 years whereas in NB-UVB group age of the patient ranges from 18-65 years. The mean age of patient with standard deviation (S.D) in PUVA group is 41.06±13.63 whereas in NBUVB is 34±12.80, this variation in age group is not statistically significant. Similar age parameters are found in study by Bhatnagar *et al*.,[59] and study by Sami Sasi Yones, *et al*.[58]. (Table: 1&2)

In this study, there are 4 males and 11 females in PUVA group and 5 males and 10 females in NBUVB group. Similar male to female ratio found in study by Bhatnagar *et al*.[59], (Table:2). This higher number of female

patients in each group is probably due to increased cosmetic concern expressed by female patients.

In this study all the 30 patients were of Vitiligo vulgaris type.Most of the patients had Vitiligo patches over face,upper and lower limbs. Only some patients had trunk involvement. In the study by Bhatnagar et al.[59], in PUVA group 23 patients had Vitiligo vulgaris whereas one patient each had focal and acrofacial involvement and in NBUVB group all 25 patients had Vitiligo vulgaris.

In this study, the duration of disease in PUVA group ranges from 2 yrs to 15 yrs whereas in NBUVB group 2 yrs to 10 yrs. Mean duration of disease in PUVA group is 4.53±2.19 whereas in NBUVB group is 4.96±3.67.(Table: 1,3). The difference between the mean duration of Vitiligo in both groups was statistically not significant ($p>0.05$). Study by Bhatnagar et al.[59], mean duration of treatment in PUVA group is 4.36±2.94 whereas in NBUVB is 11.24±7.6 which is not concurrent to this study.

The body surface area affected by vitiligo in PUVA group ranges from 13% to 48% whereas in NBUVB 11% to 47%. Mean body surface area affected by vitiligo in PUVA group is 24.9±9.95 whereas in NBUVB is 23.83±11.96 (Table:4). The difference of mean surface area affected by Vitiligo between two groups was statistically not significant. Similar body

surface area involvement is seen in Study by Bhatnagar et al.[5a.] and parsad et al.

The duration of treatment taken by PUVA group ranges from 6 months to 8 months whereas in NBUVB it is 6 months to 10 months. The mean duration of therapy in PUVA group is 6.85±0.99 whereas treatment in NBUVB group 7.26±1.22. Which is comparable to the duration of treatment seen in study by Sami Sasi Yones, *et al*.[58]. But, in the study by Bhatnagar et al.[59,] , it is slightly less (6.3±1.71 in NBUVB, 5.64±1.8 in PUVA)

In this study, comparing the demographic and disease parameters between the two groups, no statistically significant differences were found. Which is comparable to the study done by Sami Sasi Yones, *et al*[5.] In the study by Bhatnagar *et al*.[59] also no statistically significant differences were found in any of the variables except for total disease duration, which was more in the NBUVB group(Table:1).

Treatment response:

In this study, time taken for initial repigmentation ranges from 4 weeks to 12 weeks in both groups. The average time taken for initial repigmentation in NB-UBV groups is 6.6±2.6 weeks whereas in PUVA group is 6.93±2.8 weeks. This is similar to the study by Bhatnagar *et al*,[59]. This difference was not statistically significant(Table:5).

None of the patient in both groups showed 100%(grade 5) response and also 0%(Grade 0) response. Overall, 11 persons(73.3%) are in grade 3 and 4 treatment response in NB-UVB group where as only 7 persons(46.6%) in PUVA group. Four persons (26.5%) in NB-UVB group showed grade 4 response where as in PUVA group there were no person in the grade 4 response seen at the end of the treatment. (Table 10). However after excluding the resistant sites that is hands and feet, 1 person in the PUVA group and 5 persons in the NB-UVB group showed grade 4 response. Overall 11 persons(73%) are in grade 3 and 4 response in NB-UVB group whereas only 10 persons(67%) in PUVA group after excluding resistant sites (Table:11). This shows in NB-UVB group the treatment response is better than PUVA group. Similar report were found in study by Parsad et al.

In this study, (Table: 6, 7&13) comparing the treatment response at five months there is no statistically significant difference (PUVA 1.45 NBUVB 1.71). Mean grade of treatment response at the end of the treatment in PUVA therapy is 2.01 whereas in NBUVB 2.5. (Table8,9&13) Comparing the treatment response at end of treatment there is statistically significant difference between both groups. Study by Parsad et al., showed similar result. This is in contrary to study by Bhatnagar et al. Even after excluding the resistant sites i.e hands and feet ‘,the mean grade of treatment response at 5 months there is no statically significant difference. Mean grade of

treatment response at the end of the treatment after excluding resistant sites in PUVA therapy is 2.34 whereas in NB-UVB it is 2.9. This difference is statistically significant(Table: 14) study by Bhatnagar et al and Parsad et al showed similar results.

Minimal mean grade of treatment response (Grade 1) was seen in hands and feet in both groups (Table :12). Comparable results were found in the study by Bhatnagar *et al*[59], Sami, sasi yonus et al also. Area wise assessment of repigmentation showed greater pigmentation seen in face and trunk lesions in the NBUVB group. In the PUVA group greater pigmentation seen in neck and limb lesions. In this study the lower grade of facial repigmentation seen in PUVA may probably due to the fact that in the face only lips are commonly affected by Vitiligo in this group.

Colour match in Vitiligo patches after NBUVB treatment was exactly same as that surrounding skin in 13 patients (86%). Only in 2 patients (14%) repigmentation is darker than surrounding skin that too only in the margins. In study by Sami Sasi Yones *et al*.[58], all patients had exactly the same colour compare to the surrounding skin in NBUVB group. Study by Bhatnagar et al.[59,] 22 persons (88%) showed same colour match. This colour match was cosmetically very appealing to the patient which improves the psychological satisfaction felt by the patient. (Table : 15)

In PUVA group, only in 7 patients (46%) the colour match is same as that of surrounding skin, whereas in 8 patients (54%) the colour match was darker than the surrounding skin. Study by Bhatnagar *et al.*,[59] in PUVA group 11 (44%) patients out of 25 had somewhat darker colour. In the study by Sami sasi Yones *et al*[58]., in PUVA group 14 (61%) patients out of 25 had ecact colour match. Considering the colour match, there is statistically significant difference between both groups $p<0.05$. (Table:15)

Excellent satisfaction was seen in 1 patient in NBUVB group, but no patients in PUVA group. Nine patients in NBUVB group and 6 patients in PUVA group experienced good satisfaction. Considering the psychological satisfaction, there is no statistically significant difference between both groups $p<0.05$.

Side effects are minimal in both groups. None of the patient stopped the treatment because of side effects in both groups. Itching is the common side effect noticed in NBUVB group which occurred in 4 patients (26%). One patient developed blisters in lip on first day of therapy which cleared within 2 days. Side effect like Nausea and vomiting were not noticed NB UVB group. Study by Bhatnagar *et al.*[59] 9 patients(36%) experienced side effects (herpes labialis in 4 patients, mild to moderate itching in 3 patients, urticaria in 1 patients and symptomatic dermographism in 1 patient) but Herpes labialis is not noticed in this study.

In PUVA therapy side effect were noticed in 6 patients (40%). Nausea and vomiting occurred in 2 patients, itching and burning sensation were noted in 4 patients. However, the Nausea and vomiting is not severe enough to stop the therapy. They were managed by giving Psoralen along with food and symptomatic treatment. Study by Bhatnagar et al.[59],1 13 patients(52%) experienced side effects. (Itching in 4 patients, sedation in 3 patients, xerosis in 3 patients, Exacerbation of acne lesions in 3 patients, nausea in 2 patients). Considering the side effect, there is no statistically significant difference between both groups ($p<0.05$).

There is a consistent improvement in treatment response as the duration of therapy increases. (Table:16). Study by Harikrishnan kumar et al[11] it is stated that good response is directly associated with more number of exposure, cumulative dose and good compliance. Our study also established this fact.

Comparing NBUVB therapy with PUVA therapy, like many other studies, our study also establish the fact that both PUVA therapy and NBUVB therapy are efficacious in treatment of Vitiligo. NBUVB therapy is superior to PUVA therapy in term of mean degree of repigmention colour match and psychological satisfaction experienced by the patient.

SUMMARY

This open prospective comparative study was conducted to compare the safety and efficacy of PUVA therapy and NBUVB therapy in the treatment of Vitiligo.

The demographic and disease parameters were comparable between each group.

The difference in the time taken for initial repigmentation between both groups is not statistically significant.

There is consistent improvement in the treatment response in each group from onset as the duration of treatment increases.

At the end of 5 months, the mean grade of treatment response is slightly better in NBUVB group compared to PUVA group, however it is statistically not significant.

At the end of treatment, the mean grade of treatment response in NBUVB group is higher than that in the PUVA group. This difference is statistically significant.

The colour match same as that of surrounding skin is seen in 86% of patient in NBUVB group whereas only 46% in PUVA group. This same colour match is cosmetically very appealing to the patients and it increases the psychological satisfaction.

The mean grade of treatment response increases in both groups after excluding the resistant sites (i.e., hands and feet).

Minimal response is seen in hands and feet in both groups. Face and trunk lesions showed maximal response in NBUVB. PUVA group neck lesion showed maximal response.

Patient in NBUVB group had greater psychological satisfaction compare to PUVA group. However, the difference is not statistically significant.

Patient in NBUVB group had lesser side effects than PUVA group. However, it is not statistically significant.

CONCLUSION

The NBUVB groups showed better response in all the treatment response parameter compared. There was a statistically significant improvement seen in mean grade of treatment response at the end of treatment and the colour match. In the treatment of vitiligo NBUVB therapy is superior to PUVA therapy. However studies with larger group of patient and longer duration of treatment and follow up are essential to reveal further differences or to confirm the result of this study.

BIBLIOGRAPHY

1. Natural and Synthetic Furanocoumarins as Treatment for Vitiligo and Psoriasis Filomena Conforti1,*, Mariangela Marrelli1, Federica Menichini1, Marco Bonesi *Current Drug Therapy*, 2009, *4*, 38-58
2. Childhood vitiligo – an overview, Prof. Jayakar Thomas, e-Journal of the Indian Society of Teledermatology, 2008;Vol 2, No.4,
3. Spritz RA. The genetics of generalized vitiligo. Curr Dir Autoimmun 2008;10:244–257.
4. Howitz J, Brodthagen H, Schwartz M, Thomsen K. Prevalence of vitiligo. Epidemiological survey on the Isle of Bornholm, Denmark. Arch Dermatol 1977;113:47–52
5. Boisseau-Garsaud AM, Saint-Cyr I, Quist D, Arveiler B, Garsaud P. Familial aggregation of vitiligo in the French West Indies (Isle of Martinique). Eur J Dermatol 2001;11:554–556
6. Lu T, Gao T, Wang A, Jin Y, Li Q, Li C. Vitiligo prevalence study in Shaanxi Province, China. Int J Dermatol;46:47–51.
7. Mehta NR, Shah KC, Theodore C, Vyas VP, Patel AB. Epidemiological study of vitiligo in Surat area, South Gujarat. Indian J Med Res 1973;61:145–154.
8. Das SK, Majumder PP, Chakraborty R, Majumdar TK, Haldar B. Studies on vitiligo. I. Epidemiological profile in Calcutta, India. Genet Epidemiol 1985;2:71–78.
9. Astanet J, Ortonne JP. Pathophysiology of vitiligo. Clin Dermatol, 15:845-851, 1997.
10. Whitton ME, Ashcroft DM, Barrett CW, Gonzalez U. Interventions for vitiligo. *Cochrane Database Syst Rev*. 2006;1:CD003263

11. Evaluation of narrow-band UVB phototherapy in 150 patients with Vitiligo Y Hari Kishan Kumar, G Raghu Rama Rao, K.V.T Gopal, G Shanti, K VeerabhadraRao
12. Narrowband–UV-B PhotoTherapy in Dermatology,Sunil Dogra, Amrinder: Indian Journal of Dermatology, Venerology & Leprosy July-August 2004:volume 70 :Issue 4
13. BB, Tarwade YV, Dambre GM,. Vitiligo monograph. *Pune Gokhale Mediservice Trust; 1989.*
14. Sandipan dhar, Pijush dutta, Rajib Malakar; Pigmentary disorders IADVL text book of dermatology vol 1 3rd edition; *RG Valia, Amit R Valia; Bhalani publisher house Mumbai India.*
15. Theories for the etiology of Vitiligo, Chris White. Bulletine for internal circulation for Vitiligo surgeon, Tan Research E- Publication.
16. Hegedus L, Heindenheim M, Gervil M, *et al.* High frequency of thyroid dysfunction in patients with vitiligo. Acta Derm Venereol 74:120-123, 1994.
17. Ongenae K, Van Geel N, Naeyaert JM. Evidence for an autoimmune pathogenesis of vitiligo. Pigment Cell Res 16:90-100, 2003.
18. Al'Abadie MS, Senior HJ, Bleeh SS, Gawkrodger DJ. Neuropeptide and neuronal marker studies in vitiligo. Brit J Dermatol 131:160-165, 1994.
19. Cucchi ML, Frattini P, Santagostino G, *et al.* Higher plasma catecholamine and metabolite levels in the early phase of nonsegmental vitiligo. Pigment Cell Res13:28-32, 2000.
20. Hara M, Toyoda M, Yaar M. Innervation of melanocytes in human skin. J Exp Med 184: 1385-1395, 1996.
21. Schallreuter Ku, Wood JM, Berger J. Low catalase levels in the epidermis of patients with vitiligo. J Invest Dermatol 97:1081-1085, 1991.

22. Maresca V, Roccella M, Roccella F, *et al.* Increased sensitivity to peroxidative agents as a possible pathogenic factor of melanocyte damage in vitiligo. J Invest Dermatol 109:310-313, 1997

23. Schallreuter KU, Moore J, Wood JM, *et al.* J Invest Dermatol Symposium Proceedings 4:91-96, 1999.

24. Dell'Anna ML, Maresca V, Briganti S, *et al.* Mithocondrial impairment in peripheral mononuclear cells durino the active phase of vitiligo. J Invest Dermatol 117:908-813, 2001.

25. Bateia PS, Mohan L, Pandey ON, *et al.* Genetic nature of vitiligo. J Dermatol Sci 4, 180-184, 1992.

26. Nath SK, Majumder PP, Nordlund JJ. Genetic epidemiology of vitiligo: multilocus recessivity cross-validated. Am J Hum Genet 55:981-990, 1994.

27. Alkhateeb A, Fain PR, Thody A, *et al.* Epidemiology of vitiligo and associated autoimmune diseases in Caucasian probands and their families. Pigment Cell Res 16:208-214, 2003

28. Bystryn JC. Immune mechanisms in vitiligo. Clin Dermatol 15:853-861, 1997.

29. Vitiligo- new etiology based treatments,Abdul Hameed, Zahida Rani, Atif Hasnain Kazmi Journal of Pakistan Association of Dermatologists 2005; 15: 252-260.

30. Le Poole IC, Das PK, van den Wijngaard RM, *et al.* Review of ethiopathomechanism of vitiligo: a convergence theory. Exp Dermatol 2:145-153, 1993.

31. Vitiligo , R. H. Huggins, R. A. Schwartz and C. Krysicka Janniger, Acta Dermatoven APA Vol 14, 2005, No 4

32. Jean paul ortonne vitiligo and other disorders of hypopigmentation 2nd edition dermatology edited by Jean L-Bolognia JosephLJorizzo RonaldP Rapini

33. Sharquie KE. Mehenna SH. Naji AA. Al-Azzawi H. Inflammatory changes in vitiligo: stage I and II depigmentation. Am J Dermatopathol 2004; 26: 108-12.

34. Update on skin repigmentation therapies in Vitiligo, Rafael Falabella and Maria I. Barona2008, journal compilation.

35. J. Dtsch. Dermatol. Ges. 5, 467–475. Mahmoud, B.H., Hexsel, C.L., and Hamzavi, I.H. (2008). An update on new and emerging options for the treatment of vitiligo.

36. Skin Therapy Lett. 13, 1–6.Shen, Z., Gao, T.W., Chen, L., Yang, L., Wang, Y.C., Sun, L.C., Li,C.Y., Xiao, Y., and Liu, Y.F. (2007).

37. Optimal frequency of treatment with the 308-nm excimer laser for vitiligo on the face and neck. Photomed. Laser Surg. 25, 418–427.

38. Schallreuter, K.U., and Pittelkow, M.P. (1988). Defective calcium uptake in keratinocyte cell cultures from vitiliginous skin. Arch. Dermatol. Res. 280, 137–139.

39. Nordlund, J.J. (2000). Depigmentation for the treatment of extensive vitiligo. In Vitiligo, S.K. Hann, and J.J. Nordlund, ed. (Luc¸on, France: Blackwell Science), pp. 207–213.

40. Behl, P.N., and Bhatia, R.K. (1973). Treatment of vitiligo with autologous thin Thiersch's grafts. Int. J. Dermatol. 12, 329–331.

41. Dr. Colin Kwok Yew Kai Consaltant Dermatologist, Natoonal Skin Centre. :Bulletin for medical practitioners

42. Pathak MA, Fitzpatrick TB. The evolution of photochemotherapy with psoralens and UVA (PUVA): 2000 BC to 1992 AD. J Photochem Photobiol B:Biol 1992;14:3-22.

43. Roelandts R. The history of photochemotherapy. Photodermatol Photoimmunol Photomed 1991;8:184-9.

44. Physical characteristics and sources of exposure to artificial UV radiation

45. UVA photo(chemo)therapy, DermNet NZ, New Zealand Dermatological society publication.

46. Gupta A K, Anderson T F. Psoralen photochemotherapy, journal of JMACAD dermatology 1987 – 17 – 703 - 734

47. Psoralens srinivas CR, Pai – Indian J Dermatol Venereol Leprology – 1997 page 276 – 287.

48. Hobert Honigsmann M.D, Rolf markes szeimies M.D, Photo chemotherapy, and Photodynamic therapy in dermatology in general medicine. 7th edition. Edited by Klaus wolff, Lowella Goldsmith. McGrawhill company. Newyork. Yr 2008

49. Phototherapy with Narrowband UVB Mark BERNEBURG, Martin RO¨ CKEN and Frauke BENEDIX Department of Dermatology, Eberhard Karls University, Tuebingen, Germany

50. Duthie MS, Kimber I, Norval M. The effects of ultraviolet radiation on the human immune system. Br J Dermatol 1999; 140: 995–1009.

51. Krutmann J, Morita A, Elmets A. Mechanisms of photo(chemo)therapy. In: Krutmann J, Honigsmann H, Elmets CA, Bergstresser PR, eds. Dermatological phototherapy and photodiagnostic methods Berlin: Springer, 2001: 56–59.

52. El Ghorr AA, Norval M. Biological effects of narrowband (311 nm TL01) UVB irradiation: a review. J Photochem Photobiol B 1997; 38: 99–106.
53. Kraemer KH, Lee MM, Scotto J. Xeroderma pigmentosum. Cutaneous, ocular, and neurologic abnormalities in 830 published cases. Arch Dermatol 1987; 123: 241– 250.
54. Gloor M, Scherotzke A. Age dependence of ultraviolet light-induced erythema following narrow-band UVB exposure. Photodermatol Photoimmunol Photomed 2002; 18: 121–126.
55. Berneburg M, Plettenberg H, Krutmann J. Photoaging of human skin. Photodermatol Photoimmunol Photomed 2000; 16: 239–244.
56. Parametric Modeling of Narrowband UV-B Phototherapy for Vitiligo Using a Novel Quantitative Tool, Iltefat Hamzavi, MD; Hem Jain, MD, FRCPC; David McLean, MD, Arch Dermatol/vol 140, June 2004
57. Njoo MD, Spiels PT, Bos JD, on surgical repigmentation therapies in Vitiligo a meta analysis of literature. Arch dermatology 1998; 134;1532-1540.
58. Randomized Double-blind Trial of Treatment of Vitiligo *Efficacy of Psoralen–UV-A Therapy vs Narrowband–UV-B Therapy Sami Sasi Yones, Dip Der, MSc, FCD; Roy A. Palmer, MA, MRCP; Trish M. Garibaldinos, RN; John L. M. Hawk, MD, FRCP* arch dermatology.
59. Comparison of systemic PUVA and NB-UVB in the treatment of Vitiligo: an open prospective study. *A Bhatnagar, AJ Kanwar, D Prasad, D De. Department of dermatology, venereology and leprology, post graduate institute of medical education and research, Chandigarh, India* JEADV ISSN 1468 – 3083.
60. Parsad D, Kanwar AJ, Kumar B. Soralen- Ultraviolet A vs. Narrow band ultra violet B phototherapy for treatment of Vitiligo. *J Eur Acad Dermatol Venereol 2006; 20; 175-177.*

61. Narrow-band UVB for the treatment of vitiligo: an emerging effective and well-tolerated therapy Amrinder Jit Kanwar, MD , Sunil Dogra, MD, DNB, MNAMS , Davinder Parsad, MD and Bhushan Kumar, MD, MNAMS. *int J of dermatology 2005* 57 – 60.

ABBREVIATION

8MOP	-	8 Methoxy Psoralens
D.f	-	Degree of freedom
H_2O_2	-	Hydrogen peroxide
HLA	-	Human Leucocyte Antigen
ICAM	-	Inter Cellular Adhesion Molecule
NBUVB	-	Narrow Band ultraviolet B
NSV	-	Non segmental Vitiligo
PG	-	Prostaglandin
PUVA	-	Psoralen Ultraviolet A
S.D	-	Standard Deviation
TMP	-	4, 5, 8 – Trimethyl psorlens
TNF α	-	Tumor necrosis factor α
VASI	-	Vitiligo Area severity Index

Comparative Study of PUVA Therapy & NBUVB in Vitiligo Vulgaris

PROFORMA

Name :	Skin OP No. :	Date :
Age :	Sex :	Occupation :
Address :		Phone :

Presenting complaint (S) :

Onset

Duration

Progression

Area of Involvement

Initial Photograph

Treatment History

History of Photosensitivity

History of Past Illness

Associated diseases

DM/HT/Thyroid disease / anemia / Other Auto immune disease

Personal History

Family History

Investigation

HB%

TC

DC

Blood Sugar (R)

Blood Urea

Creatinine

Thyroid function tests

Liver functions tests

Auto antibodies

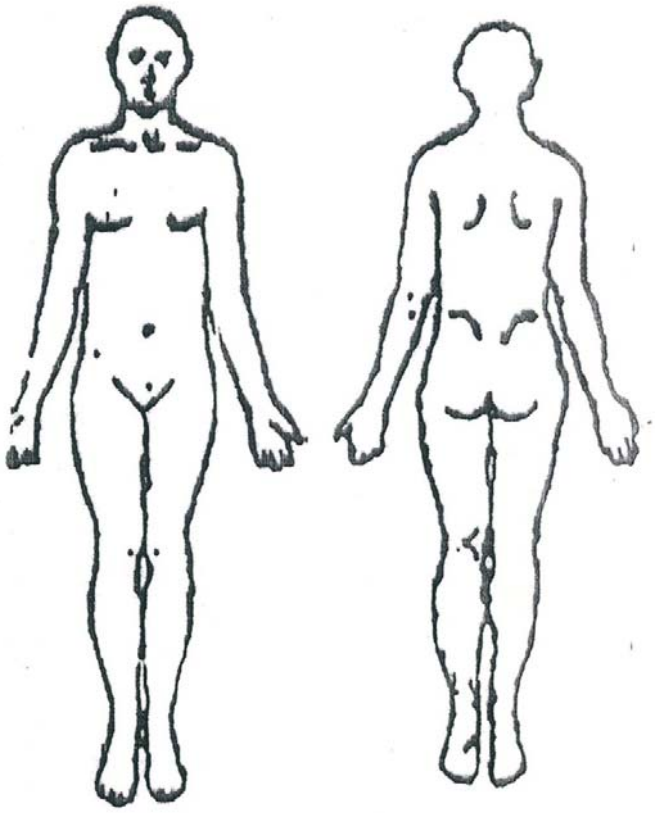
Treatment Schedule

S.No.	Date	Dose	Cumulative dose	Follow up & Remarks
1.				
2.				
3.				
4.				
5.				
6.				
7.				
8.				
9.				
10.				
11.				
12.				
13.				
14.				
15.				
16.				
17.				
18.				
19.				
20.				
21.				
22.				
23.				
24.				
25.				
26.				
27.				
28.				
29.				
30.				

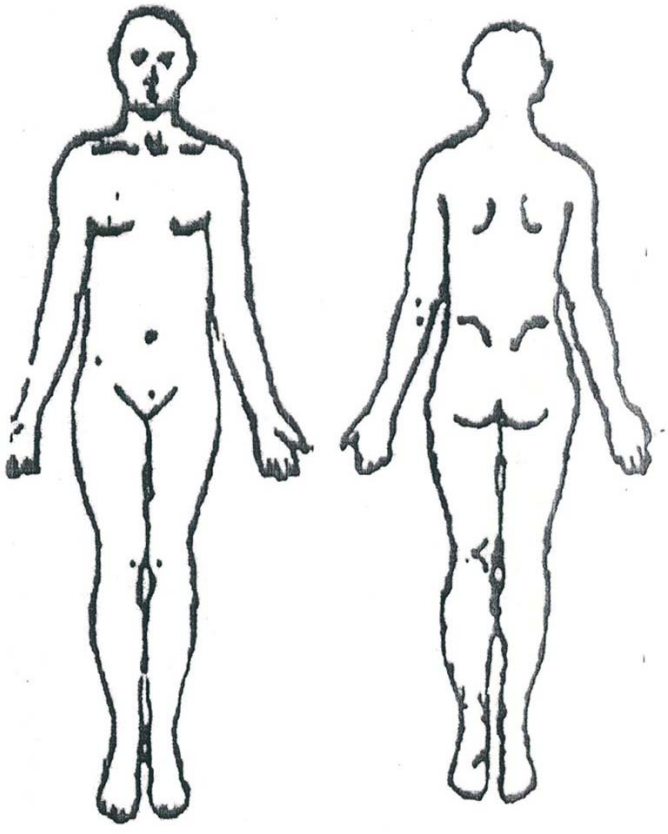
WEEKLY TREATMENT RESPONSE

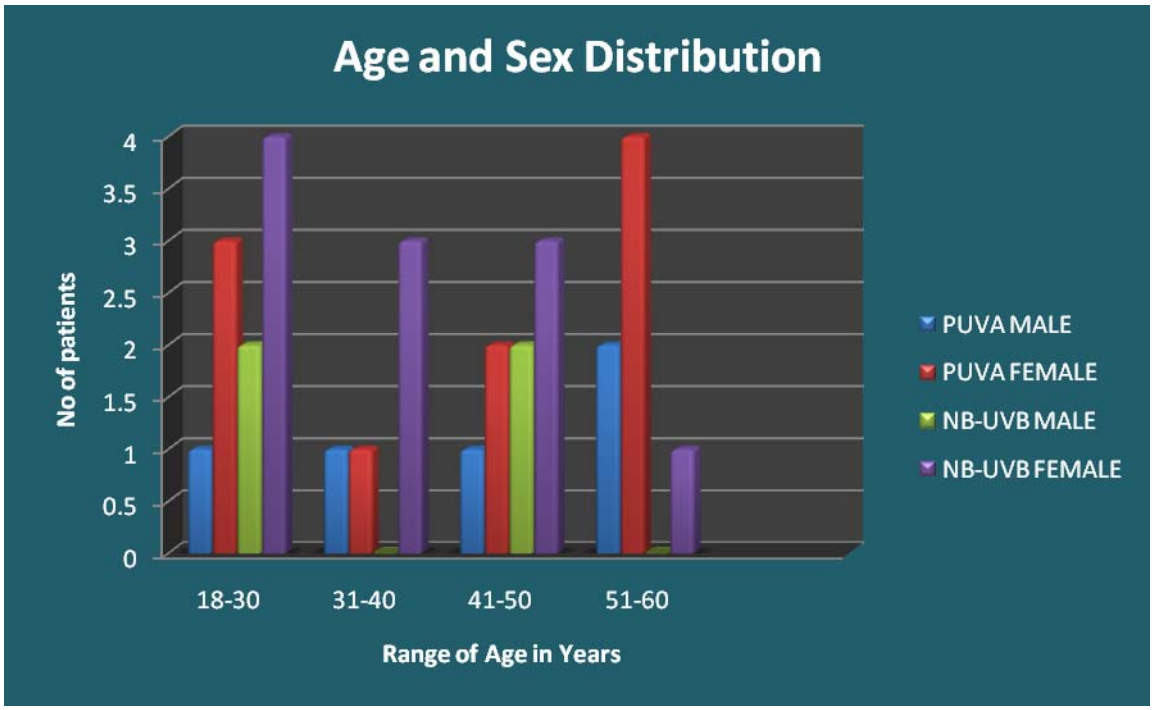
S.No.	Wks	Face	Neck	AT	PT	UL	LL	Hand	Sat	Mean
	2									
	4									
	6									
	8									
	10									
	12									
	14									
	16									
	18									
	20									
	22									
	24									
	26									
	28									
	30									
	32									
	34									
	36									

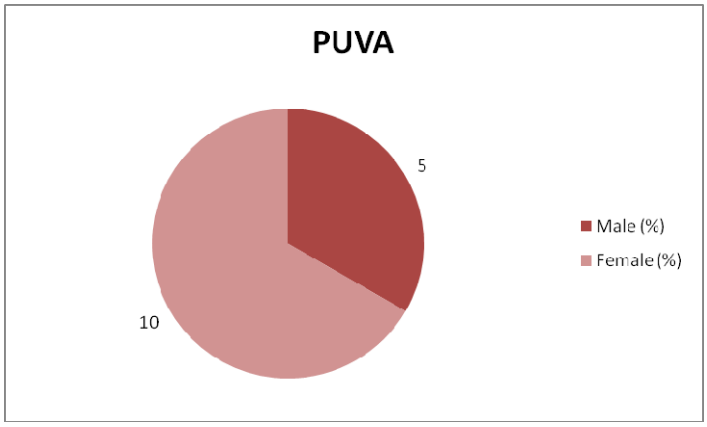
Initial surface areas affected by Vitiliogo

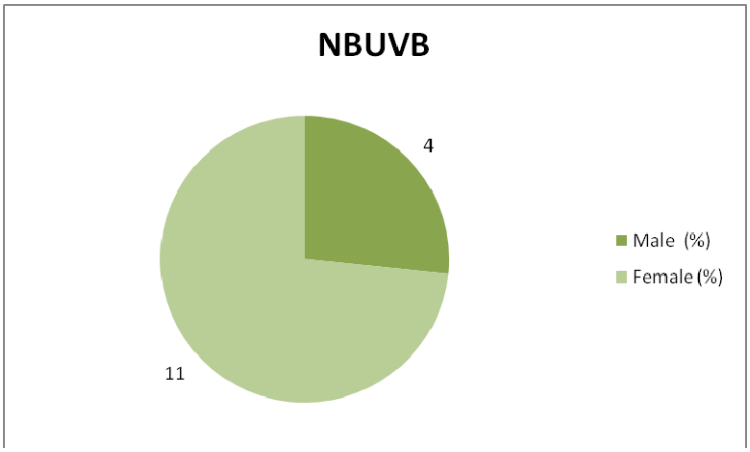


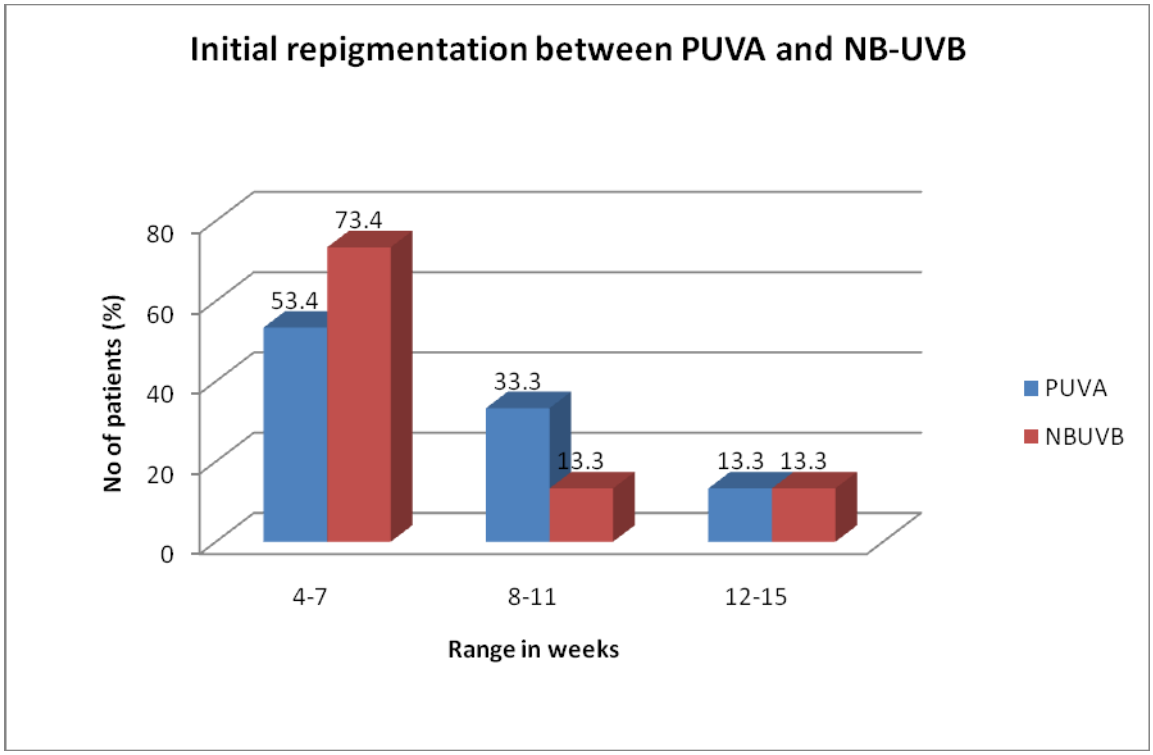
Treatment response at the end

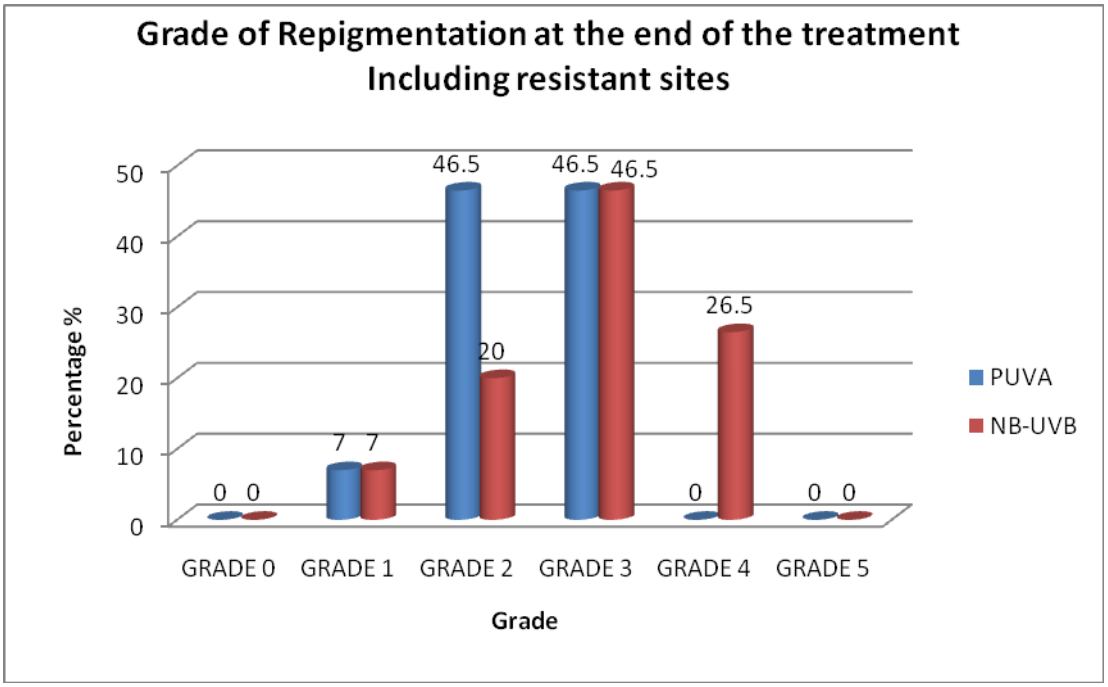


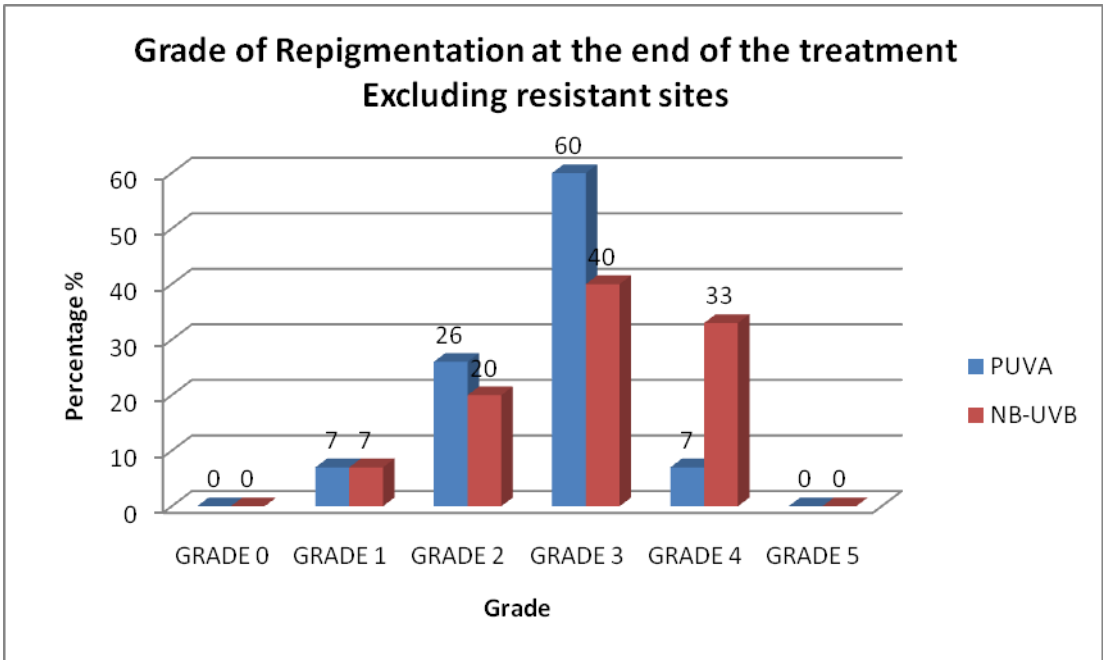

Age and Sex Distribution
No of patients
4
3.5
3
2.5
2
1.5
1
0.5
0
18-30
31-40
41-50
51-60
Range of Age in Years
PUVA MALE
PUVA FEMALE
NB-UVB MALE
NB-UVB FEMALE

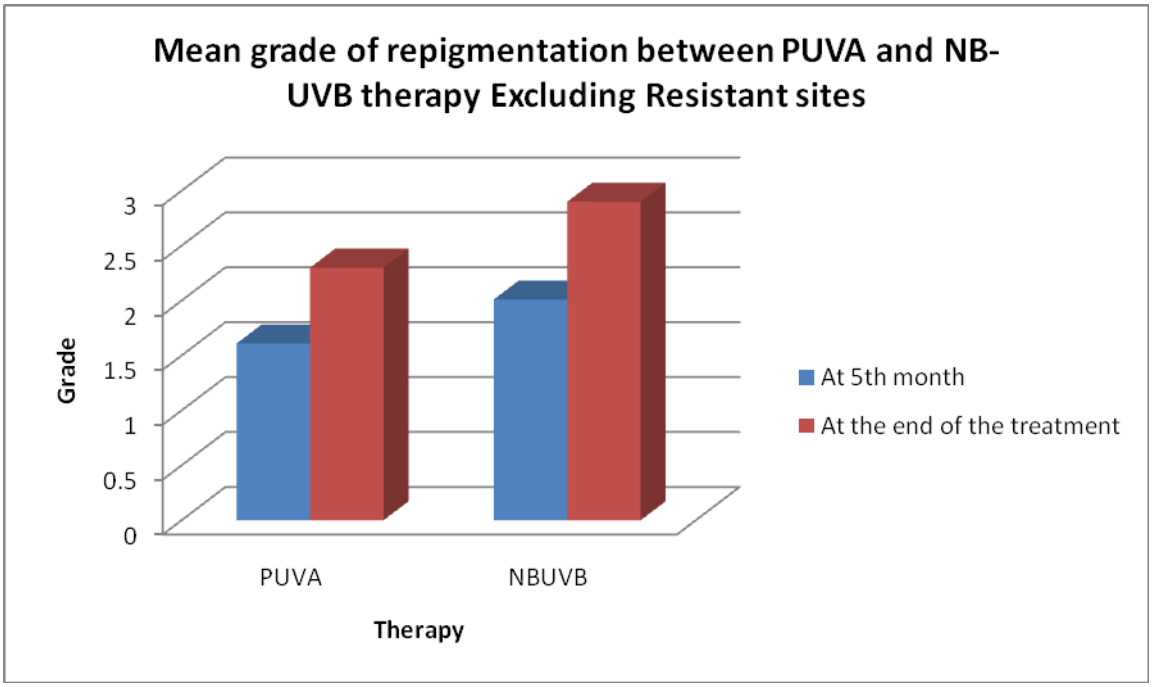

PUVA
5
10
Male (%)
Female (%)

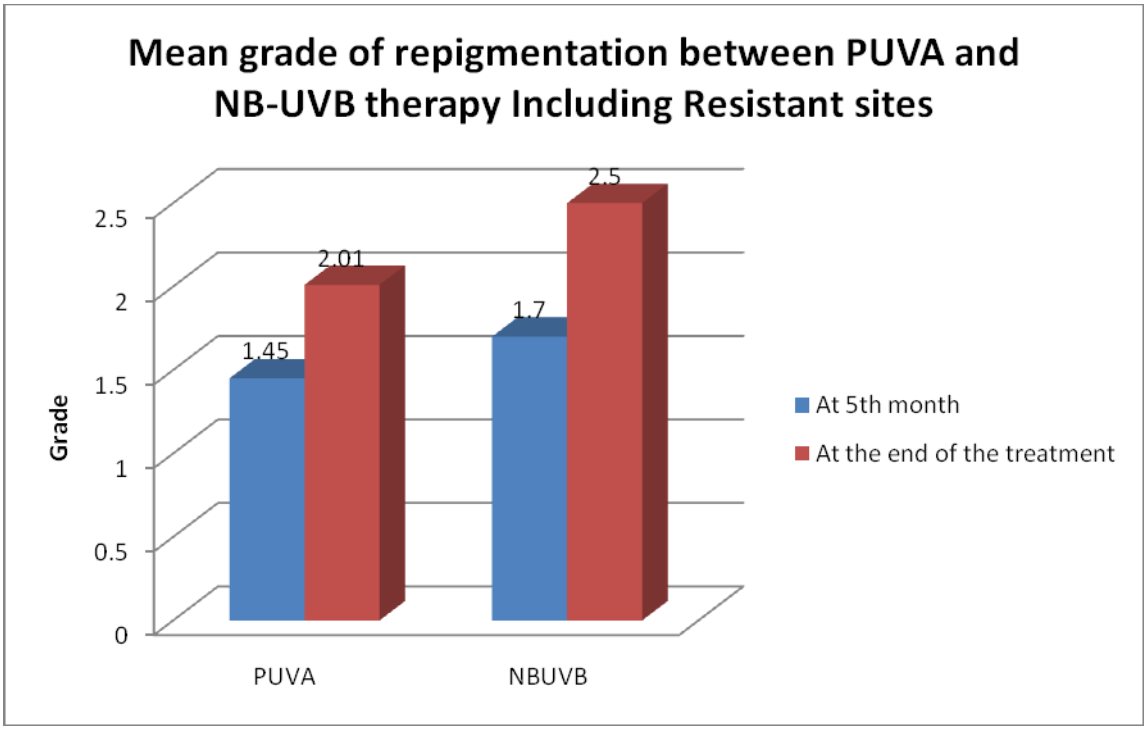

NBUVB
4
11
Male (%)
Female (%)

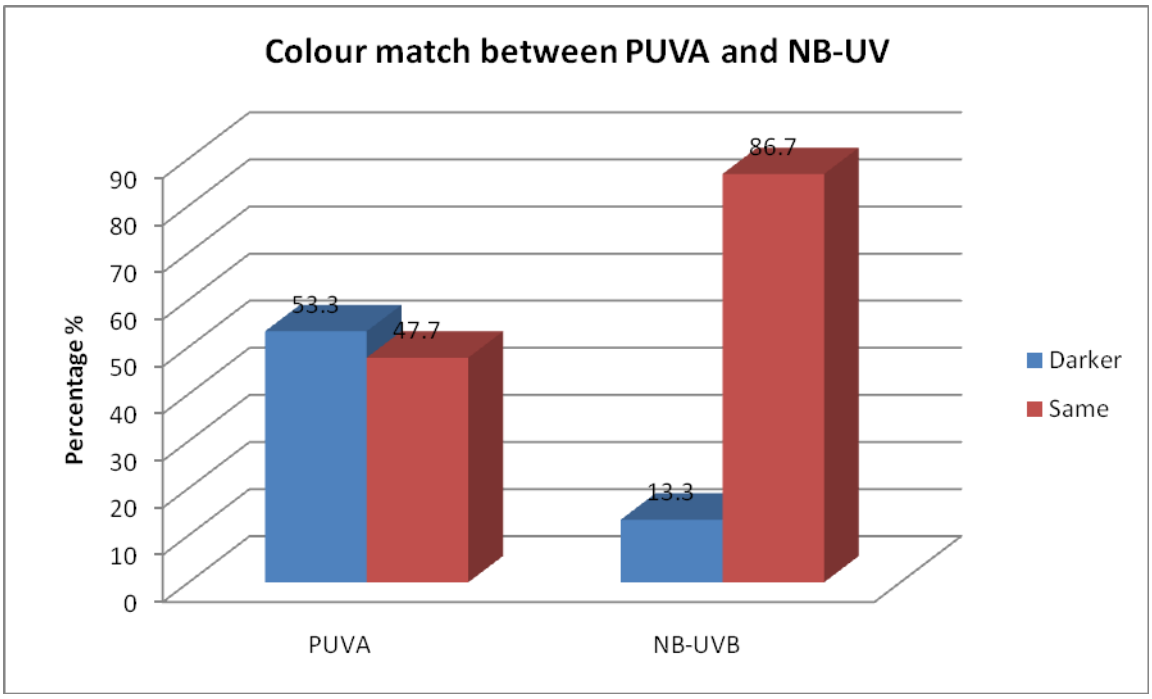

Initial repigmentation between PUVA and NB-UVB
No of patients (%)
80
60
40
20
0
73.4
53.4
33.3
13.3
13.3
13.3
4-7
8-11
12-15
Range in weeks
PUVA
NBUVB


Grade of Repigmentation at the end of the treatment
Including resistant sites
Percentage %
50
40
30
20
10
0
46.5
46.5
46.5
26.5
20
7
7
0
0
0
0
0
GRADE 0
GRADE 1
GRADE 2
GRADE 3
GRADE 4
GRADE 5
Grade
PUVA
NB-UVB


Grade of Repigmentation at the end of the treatment
Excluding resistant sites
Percentage %
60
50
40
30
20
10
0
60
40
33
26
20
7
7
7
0
0
0
0
GRADE 0
GRADE 1
GRADE 2
GRADE 3
GRADE 4
GRADE 5
Grade
PUVA
NB-UVB


Mean grade of repigmentation between PUVA and NB-UVB therapy Excluding Resistant sites
Grade
3
2.5
2
1.5
1
0.5
0
PUVA
NBUVB
Therapy
At 5th month
At the end of the treatment


Mean grade of repigmentation between PUVA and NB-UVB therapy Including Resistant sites
Grade
2.5
2
1.5
1
0.5
0
1.45
2.01
1.7
2.5
PUVA
NBUVB
At 5th month
At the end of the treatment


Colour match between PUVA and NB-UV
Percentage %
90
80
70
60
50
40
30
20
10
0
53.3
47.7
13.3
86.7
PUVA
NB-UVB
Darker
Same

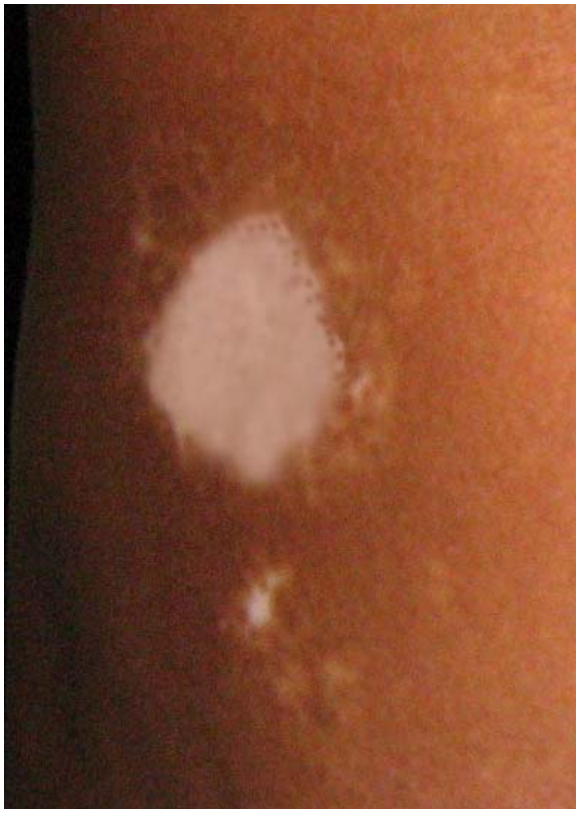
PUVA Therapy – Initial Photograph

PUVA Therapy – End of treatment - Grade 3 Response

PUVA Therapy – Initial photograph

PUVA Therapy – End of treatment – Grade 1 Response

PUVA Therapy – Initial photograph (Lower back lesion)



PUVA Therapy – End of treatment – Grade 4 Response

PUVA Therapy – Initial Photograph

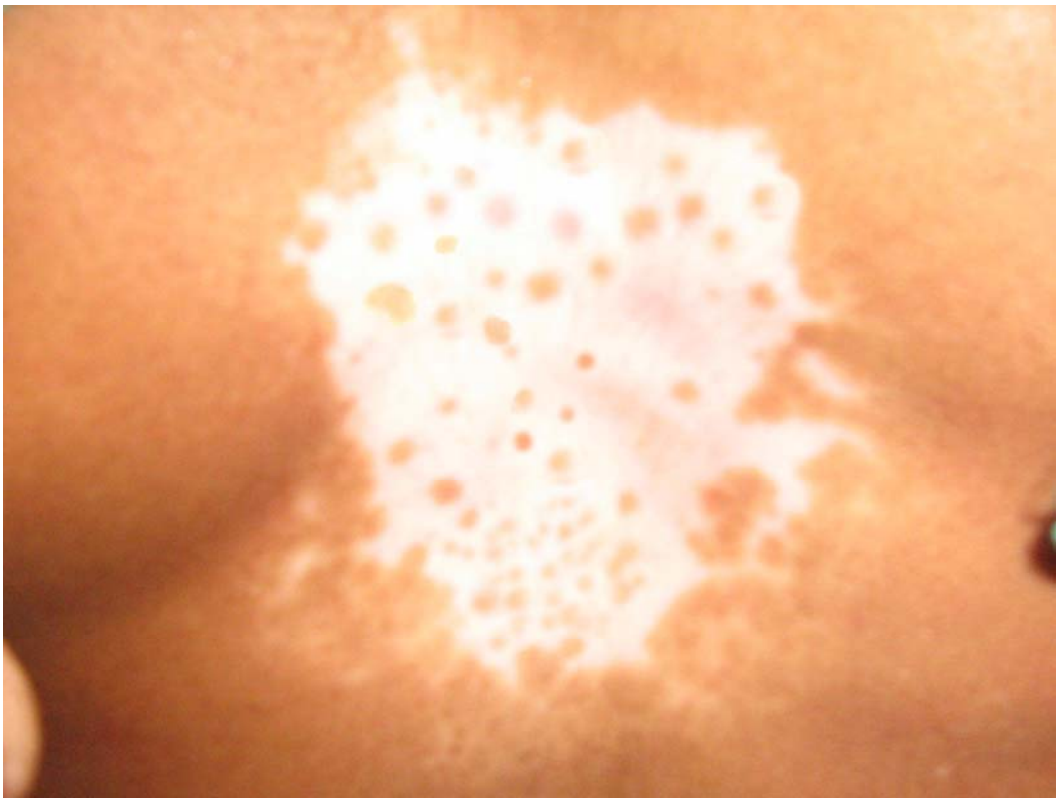
PUVA Therapy – End of treatment – Grade 3 Response

PUVA Therapy – Intial Photograph

PUVA Therapy – End of treatment – Grade 3 Response

NBUVB Therapy – 5 months – Anterior Trunk

NBUVB Therapy – End of treatment – Grade 2 Response



NBUVB Therapy – Initial Photograph

NBUVB Therapy End of treatment – Grade 3 Response

NBUVB Therapy Initial Photograph

NBUVB Therapy End of treatment – Grade 1 Response

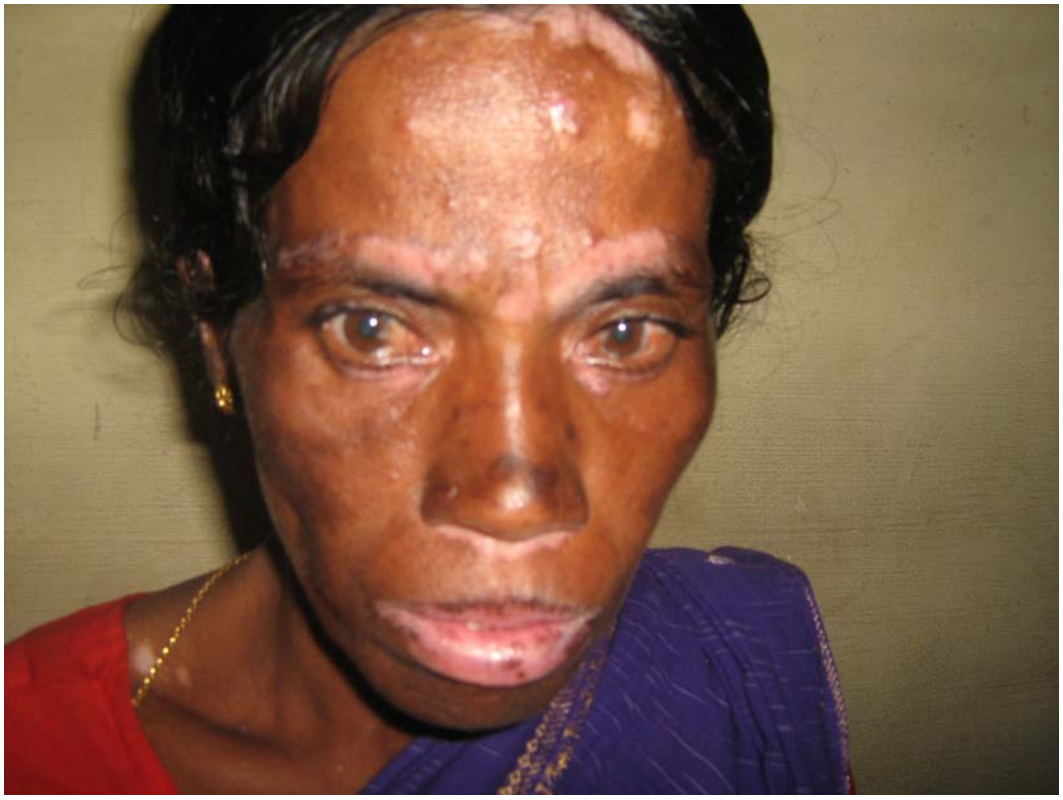
NBUVB Therapy – Initial Photograph

NBUVB Therapy – End of treatment – Grade 4 Response

NBUVB Therapy – Initial photograph (Lower Back lesion)

NBUVB Therapy – End of treatment – Grade 4 Response

NBUVB Therapy – Initial photograph



NBUVB Therapy – End of treatment – Grade 4 Response

Phototherapy Unit

(UVA & NBUVB)

NB-UVB MASTER CHART

S No	Name	Age	Sex	Occupation	Duration (Years)	Stability (Years)	Total Surface Area involved (%)	Time of Initial Repigmentation (weeks)	Family History	Associated Diseases	Investigation	Area wise Repigmentation at 5 months (Grade*)								Average Treatment Response (5 months)	Area wise Repigmentation at end of the Treatment (Grades*)								Average Treatment Response (End)	Duration Of Treatment (months)	Colour Match	Psychological satisfaction	Side Effects
												Face	Neck	Ant Trunk	Post trunk	Upper limb	Lower limb	Hands	Feet		Face	Neck	Ant Trunk	Post trunk	Upper limb	Lower limb	Hands	Feet					
1	Arunachalam	40	F	House Wife	5	2	30	4	Nil	Nil	Normal	2	-	3	2	3	2	1	1	2	5	-	5	3	4	3	1	1	3.1	10	Darker	Excellent	Blisters in lip
2	Arumugam	43	F	Labourer	15	10	10.5	6	Nil	Nil	Normal	2	-	2	-	-	-	1	1	1.5	2	-	3	-	-	-	2	2	2.25	6	Same	Good	-
3	Angela	48	F	Teacher	3	2	11	4	Nil	Nil	Normal	2	-	-	-	-	3	1	1	1.75	4	-	-	-	-	3	2	2	2.75	6	Same	Moderate	-
4	Subbu Lakshmi	20	F	Student	5	2	11	12	Nil	Nil	Normal	1	-	-	-	-	1	1	1	1	2	-	-	-	-	2	1	1	1.5	7	Same	Moderate	-
5	Gayathri Devi	18	F	Student	3	1	47	6	Nil	Nil	Normal	2	-	2	2	2	2	2	1	1.85	2	-	3	2	3	3	2	1	2.28	7	Same	Good	Itching
6	Kaliraj	25	M	Salesman	10	7	22	12	Nil	Nil	Normal	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	6	Same	Unsatisfied	-
7	Sarathi	45	M	Merchant	3	1	20	6	Nil	Nil	Normal	-	-	3	3	3	-	2	2	3.2	-	-	4	4	4	-	3	3	3.6	7	Darker	Good	-
8	Ramalingam	45	M	Merchant	7	2	32	4	Nil	Nil	Normal	2	2	2	2	2	2	1	1	1.75	3	3	2	3	3	3	1	1	2.38	8	Same	Excellent	-
9	Gomathi	60	F	House Wife	6	3	12	8	Nil	Diabetic	Normal	1	1	-	-	-	1	1	1	1	2	2	-	-	-	2	1	1	1.6	6	Darker	Good	Itching
10	Gururajan	30	M	Attender	2	1	31	4	Nil	Nil	Normal	3	2	3	3	2	2	2	1	2.25	4	4	4	4	3	3	2	1	3.25	8	Same	Good	-
11	Sujatha	18	F	Student	1.5	1	43	6	Nil	Nil	Normal	2	2	1	2	2	2	1	1	1.62	3	3	3	3	3	3	1	1	2.5	7	Same	Moderate	Itching
12	Manjula	34	F	House Wife	2	1	16	6	Nil	Nil	Normal	-	-	-	-	1	1	1	1	1	-	-	-	-	2	2	1	1	1.5	6	Same	Good	-
13	Rajashree	32	F	House Wife	3	1	18	6	Nil	Nil	Normal	-	-	3	3	2	3	1	1	2.17	-	-	4	4	3	4	2	2	3.2	8	Same	Good	-
14	Daisy	34	F	Teacher	7	3	36	7	Nil	Nil	Normal	3	2	2	2	2	2	1	1	1.87	4	3	3	3	3	3	1	1	2.63	9	Same	Good	-
15	Mary Merceline	18	F	Student	2	1	18	8	Nil	Nil	Normal	3	-	2	2	-	2	1	1	1.83	4	-	3	3	-	3	2	2	3	8	Same	Good	-

*

Grade : 0 = 0 % (No Response) Grade : 1 = 1-25% (Mild) Grade : 2 = 26-50% (Moderate) Grade : 3 = 51-75% (Good) Grade : 4 = 76-99% (Very Good) Grade: 5 = 100% (Excellent)

- = Areas not affected

PUVA MASTER CHART

S No	Name	Age	Sex	Occupation	Duration (Years)	Stability in years	Total Surface Area (%)	Time of Initial Repigmentation (Weeks)	Family history	Associated diseases	Investigation	Area wise Repigmentation at 5 months (Grades*)								Treatment Response (5 months)	Area wise Repigmentation at end of the Treatment (Grades*)								Treatment Response (End)	Duration Of Treatment (months)	Colour Match	Psychological satisfaction	Side Effects
												Face	Neck	Ant Trunk	Post trunk	Upper limb	Lower limb	Hands	Feet		Face	Neck	Ant Trunk	Post trunk	Upper limb	Lower limb	Hands	Feet					
1	Ramaiah	60	M	labourer	3	2	20	4	Nil	Nil	Normal	-	-	2	1	-	2	2	1	1.5	-	3	2	-	3	3	1	1	2.16	7	Same	Good	-
2	Mohamed Hassan	56	M	Labourer	7	4	26	8	Nil	Diabetic	Normal	2	2	-	-	-	2	2	1	1.6	2	-	-	-	3	3	1	1	2	8	Same	Good	Vomiting
3	Elizabeth	46	F	House wife	3	2	27	10	Nil	Nil	Normal	-	-	-	1	-	2	2	-	1.67	-	-	2	-	3	2	-	-	2.3	7	Same	Good	-
4	Pakiathai	46	F	Labourer	10	3	20	4	Nil	Nil	Normal	2	2	-	-	-	-	2	1	1.5	3	-	-	-	-	3	1	1	2	8	Same	Good	Itching Burning
5	Hussain	30	M	Attender	3	1	21	12	Nil	Nil	Normal	2	2	-	2	-	-	2	1	1.6	2	-	3	-	-	3	2	2	2.4	8	Darker	Good	-
6	Parvathi	55	F	House wife	6	5	38	12	Nil	Nil	Normal	1	1	-	1	1	1	1	1	1	1	-	1	1	1	1	1	1	1	6	Same	Unsatisfied	Nausea
7	Lakshmi	56	F	Labourer	4	2	13	4	Nil	Nil	Normal	1	1	-	-	-	1	1	1	1	1	-	-	-	2	2	1	1	1.4	6	Same	Moderate	Itching
8	Panchatcharam	45	M	Labourer	5	2	21	6	Nil	Nil	Normal	2	2	2	-	-	2	1	1	1.5	2	3	-	-	3	2	1	1	2	6	Darker	Moderate	-
9	Sundhararajan	31	M	Teacher	5	2	15	4	Nil	Nil	Normal	2	2	-	-	-	2	1	1	1.4	3	-	-	-	3	2	1	1	2	6	Darker	Good	-
10	Muthulakshmi	28	F	House wife	2	1	28	6	Nil	Nil	Normal	2	2	-	-	-	1	1	1	1.25	2	-	-	-	2	2	2	-	2	7	Darker	Moderate	-
11	Princy	30	F	House wife	4	1	48	4	Nil	Nil	Normal	2	2	-	2	2	3	3	2	2.14	3	-	3	3	4	4	2	1	2.85	8	Darker	Good	-
12	Regina banu	18	F	Student	2	1	38	6	Nil	Nil	Normal	2	2	1	1	-	-	1	1	1.17	2	2	2	-	-	2	1	2	1.83	7	Darker	Unsatisfied	Itching, burning
13	Sundari	35	F	House wife	4	2	26	8	Nil	Nil	Normal	2	2	-	-	-	2	2	1	1.75	3	-	-	-	3	3	2	2	2.6	8	Darker	Good	-
14	Subathra devi	25	F	House wife	3	2	16	8	Nil	Nil	Normal	2	2	2	-	-	1	-	1	1.5	2	3	-	-	2	-	2	-	2.25	6	Same	Moderate	Itching
15	prema	55	F	Labourer	7	4	15	8	Nil	Nil	Normal	-	-	2	-	-	1	1	1	1.2	-	2	-	-	2	1	1	1	1.4	6	Darker	Moderate	-

*

Grade : 0 = 0 % (No Response) Grade : 1 = 1-25% (Mild) Grade : 2 = 26-50% (Moderate) Grade : 3 = 51-75% (Good) Grade : 4 = 76-99% (Very Good) Grade: 5 = 100% (Excellent)

- = Areas not affected