“PALMOPLANTAR PSORIASIS – A COMPARATIVE THERAPEUTIC STUDY”

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(BRANCH XX)

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CERTIFICATE

Certified that this dissertation titled **"PALMOPLANTAR PSORIASIS – A COMPARATIVE THERAPEUTIC STUDY"** is a bonafide work done by **Dr. R. SATHYA NARAYANAN,** Post graduate student of the Department of Dermatology, Venereology and Leprosy, Madras Medical College, Chennai – 3, during the academic year 2012 – 2015. This work has not previously formed the basis for the award of any degree.

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The dissertation entitled **"PALMOPLANTAR PSORIASIS – A COMPARATIVE THERAPEUTIC STUDY"** is a bonafidework done by **Dr. R. SATHYA NARAYANAN** at Department of Dermatology, Venereology and Leprosy, Madras Medical College, Chennai – 3, during the academic year 2012 – 2015 under the guidance of **Prof.Dr.C.JANAKI M.D.,DD.,** Professor, Department of Dermatology, Madras Medical College, Chennai -3. This dissertation is submitted to The Tamil Nadu Dr. M.G.R. Medical University, Chennai towards partial fulfillment of the rules and regulations for the award of M.D Degree in Dermatology, Venereology and Leprosy (BRANCH – XX)

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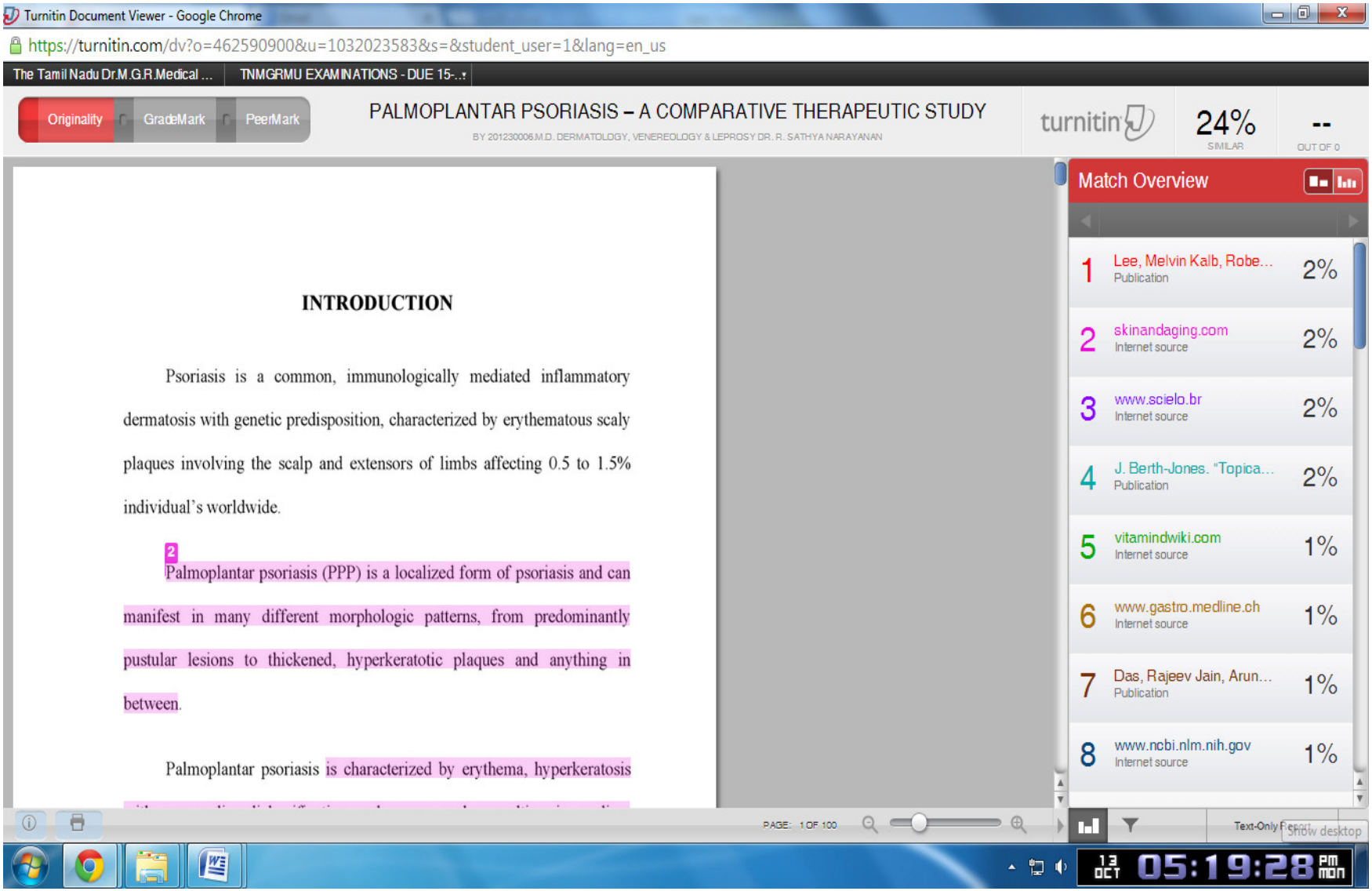
CONTENTS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INTRODUCTION
Psoriasis is a common, immunologically mediated inflammatory dermatosis with genetic predisposition, characterized by erythematous scaly plaques involving the scalp and extensors of limbs affecting 0.5 to 1.5% individual's worldwide.
2
Palmoplantar psoriasis (PPP) is a localized form of psoriasis and can manifest in many different morphologic patterns, from predominantly pustular lesions to thickened, hyperkeratotic plaques and anything in between.
Palmoplantar psoriasis is characterized by erythema, hyperkeratosis
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"PALMOPLANTAR PSORIASIS – A COMPARATIVE THERAPEUTIC STUDY"

ABSTRACT

INTRODUCTION

Psoriasis is an immunologically mediated inflammatory dermatosis characterized by erythematous scaly plaques, extremely variable in clinical manifestations ranging from innocuous lesions to life threatening pustular & erythrodermic psoriasis. Palmoplantar psoriasis present as hyperkeratotic plaques with fissures leading to significant disability. Palmoplantar psoriasis can managed with either topical agents, phototherapy or systemic agents

AIMS AND OBJECTIVES

1) To study the therapeutic efficacy of a)oral methotrexate, b)hand & foot phototherapy using NBUVB, c)topical calcitriol with clobetasol propionate ointment .
2) To do clinical evaluation using PASI scoring and assess quality of improvement using DLQI.

MATERIALS AND METHODS

Sixty patients with palmoplantar psoriasis were randomly selected. Clinical examination and necessary investigations were done and PASI scoring calculated to assess the area involved. Patients were grouped under three groups.

Group A patients were put on calcipotriol with clobetasol propionate ointment. Group B patients had hand and foot NB-UVB. Group C patients were put on tablet methotrexate.

OBSERVATION AND RESULTS

Thirty three patients were males with male to female ratio of 1.22:1.Mean age of patients was 36. Mean duration of illness was 11months. Most of the patients were manual labourers. 36 patients had lesions over palms and soles, 9 palms alone and 15 involving soles. Mean PASI reduction at 16weeks was maximum with methotrexate. Compliance was good with methotrexate and topical group. Relapse cases were seen with methotrexate.

CONCLUSION

There is no significant change in clinico-epidemiology and presentation of palmoplantar psoriasis. Methotrexate is the most efficacious modality in treatment of palmoplantar psoriasis.

INTRODUCTION

Psoriasis is a common, immunologically mediated inflammatory dermatosis with genetic predisposition, characterized by erythematous scaly plaques involving the scalp and extensors of limbs affecting 0.5 to 1.5% individual's worldwide.

Palmoplantar psoriasis (PPP) is a localized form of psoriasis and can manifest in many different morphologic patterns, from predominantly pustular lesions to thickened, hyperkeratotic plaques and anything in between.

Palmoplantar psoriasis is characterized by erythema, hyperkeratosis with surrounding lichenification and coarse scale, resulting in peeling, blistering, crusting, fissuring and bleeding. These symptoms may significantly interfere with activities, inhibiting patients from closing their hands or walking comfortably on their feet, leading to major disability and reduction in quality of life.

Palmoplantar lesions are frequently associated with psoriatic plaques elsewhere, but can occur in isolation also. In the absence of generalized psoriasis, Palmoplantar psoriasis may present similarly to eczematous forms

of dermatitis, such as irritant or allergic contact dermatitis, dyshidrotic eczema, atopic eczema, mycosis fungoides, fungal infections, and palmoplantarkeratoderma, making the diagnosis difficult. This study aims to explore the available data on treatment of palmoplantar psoriasis and its unique challenges.

Review of Literature

REVIEW OF LITERATURE

Behcet described psoriasis as an antidote to dermatologists' ego. It still remains the most baffling of dermatoses, proving to be the most vulnerable point in their armor as experts. Dermatologists of today can look with suspicion at masters of yesterday as apart from diagnosis and palliative treatment, nothing much really has been accomplished in the management of disease [1]. Maybe this is the reason why physician by the name Wilson rightly quoted "Psoriasis is not a disease on which to build a medical reputation"

Psoriasis is as old as mankind. Despite its frequency, visibility and chronicity, there is very little literature that we can draw from the works of ancient physicians. In the 18th century, after the descent of protodermatologists, there evolved a new generation of dermatologists who started describing the disease more often than not, after which Psoriasis became a distinct entity [2].

Hippocrates (460-377 BC), father of western medicine, in the golden age of greek science, described some itchy lesions over eyelids and genitals for which he used coal tar and climate as treatment. But this condition was

undoubtedly not psoriasis. Stickler et al grouped various skin conditions under the term of 'lopoi', meaning scale and coined the word 'alphos' and 'leukos' for some skin diseases with maculae but doubtless not for psoriasis[2].

Celsus in first century AD, in the book "De re medicalibriocto" described lesions which appeared on skin of extremities and nails. He suggested Pitch and Sulphur as treatment. During these times and later, Psoriasis was often confused with Syphilis, Leprosy and other skin diseases[2].

Roman encyclopedist Pliny, in his book, "NaturalisHistoria" mentions the word psora for which he suggested Cucumber as treatment. Galen (131-201 AD) used the word "Psoriasis" for itchy, scaly eruptions around eyelids and scrotum which was probably seborrheic dermatitis[2].

HeironymusMercurialis (1530-1606 AD) in his work " Demorbiscutaneis et omnibus corporishumaniexcrementis " described psoriasis under the name of " Lepragrecorum " , the other being " Psora Leprosa"[2].

English physician Robert Wilan(1757-1812) termed Psoriasis for the papulosquamous disease under the order “squamae” together with leprosy, pityriasis and icthyosis. He described different forms of psoriasis namely guttata, diffusa, gyrata, palmaria, unguium and inveterata[3].

Ferdinand Von Hebra (1806-1880) from Austria, clearly divided psoriasis from leprosy and believed in Arsenic for its treatment[2].Besnier and later Charles Bourdillon described psoriatic arthritis[2].

Despite continuing disputes, dermatology and more so Psoriasis in particular, saw tremendous growth and improved upon introduction of new histopathological classifications[3].

Leo Von Zumbusch (1884-1940) first described GeneralisedPustular Psoriasis in 1910[4]. Later in the year 1936, Barber Königsbeck described Psoriasis Palmoplantaris and differentiated it from pustulosis of palms and soles[5].

Other important landmarks related to psoriasis were

1872 – Heinrich Köbner – Kobner's Phenomenon[6]

1885 – Heinrich Auspitz – Auspitz's sign[7]

1878 – Balmanno Squire – Chrysaeobin[8]

1898 – William.J.Munro – Munro's microabscesses[9]

1916 – Pau Gerson Unna – Use of Anthralin in treatment[10]

1925 –Goeckermann – Combination of Coal Tar with UV-B[11]

1926 –Wornoff – Wornoff ring[12]

1927 – FranjoKogoj – Spongiform pustules of Kogoj[13].

1953 – John Ingram – Dithranol regimen[14]

1970 – Leavall – Treatment with Hydroxyurea[15]

1974 – Parrish – Use of 8-methoxypsoralen with UV-A[16]

1976 – Fischer – UV-B[17]

1986 – Morimoto – Use of Calcipotriol (Vitamin D analogue) [18]

2003 – Alefacept – treatment of psoriasis[18]

PSORIASIS – CURRENT SCENARIO

Psoriasis is seen globally. Prevalence ranges somewhere between 0.1% - 3% in various studies conducted all over the world[18]. With the life expectancy being comparable to normal population and the disease being persistent and chronic, the incidence of psoriasis increases with age[19].

The incidence ranges from 0.3% in China, 1.4% in United States, 2.3% in Sweden and 2.8% in France[19].

In India, incidence lies between 1% - 6% as reported from various dermatology clinics[20-24].

Mean age of incidence in males were 36.9±15.10 and in females it was found to be 29.34±15.10 [24]. There must arise suspicion about family history if the onset is earlier[25].

Indian studies showed higher prevalence in males(2.5%) than females(0.8%) [21,22].

Clinical presentation of psoriasis can be classified into two types,

- **Type 1 :** hereditary form, more common, more severe, strongly associated with HLA-Cw6 with increased incidence in 1st and 2nd decade[26].

- **Type 2:** sporadic form, less common and less severe, no HLA association affecting those in 3rd and 4th decade[26].

ETIOLOGY AND PRECIPITATING FACTORS:[27]

Psoriasis is a complex disease that its exact etiology is poorly understood. However there are numerous factors which can precipitate psoriasis namely,

1. Trauma

   Trauma may be of any form;

   a) Physical

   b) Chemical

   c) Mechanical : heavy labourers

2. Infections [27]

   Beta hemolytic streptococcal infections – Upper respiratory tract infections, tonsillitis.

HIV infection is proven to exacerbate psoriasis[27]

3. Season[28]

   Winter exacerbates psoriasis whereas summer is known to bring about remission

4. Metabolic factors[29]

   Hypocalcemia precipitates psoriasis, particularly pustular psoriasis.

5. Endocrine factors[30]

   Psoriasis reaches its peak during puberty and menopause. Similarly studies have shown that psoriasis remits during pregnancy and exacerbates during post-partum period.

6. Stress[31]

   Stress is directly related to psoriasis and psoriasis in turn, will lead to depression which in turn will flare up psoriasis.

7. Alcohol[32]

   Alcoholics with psoriasis will consume excessive amounts of alcohol which will increase severity of the disease.

8. Drugs[33]

Drugs precipitating psoriasis are

a) Beta blockers
b) Antimalarials
c) Lithium
d) Anti convulsants
e) NSAID's
f) Sudden withdrawal of systemic steroids, super potent steroids, coal tar, dithranol and phototherapy
g) Others: amiodarone, clonidine, digoxin, gemfibrozil, potassium iodide, penicillin andterfinadine.

9. Smoking[28]

Men who are smokers do not show an increased risk but those already having psoriasis will have increased expression of the disease over the extremities if they smoke more than 10 cigarettes per day.

10. Metabolic syndrome[28]

Psoriasis being an immunologically mediated inflammatory skin disease, many studies substantiate the association of psoriasis with

comorbidities like diabetes, hypertension, lipid abnormalities, stroke and myocardial infarction. In a study by Anandan et al, certain parameters like abdominal obesity, hypertension and elevated triglycerides were found to be significantly associated with moderate to severe disease.

Metabolic Syndrome and psoriasis have certain immunological mechanisms in common. Psoriasis is associated with elevated levels of IL-6, plasminogen activator inhibitor type 1 and TNF-α . The elevated levels of these inflammatory mediators is associated with visceral adiposity. Thus the accumulated intra-abdominal fat starts to act as an endocrine organ secreting adipocytokines which affect glucose metabolism and internal biology of vascular endothelium and promotes inflammation. Leptin, secreted by adipocytes, is found to be elevated in psoriasis. It modulates the type 1 and 2 T-helper cells by regulating cytokine expression a significant role in acute and chronic inflammation via regulation of cytokine expression that modulates the type 1 and 2 T-helper cells. Metabolic syndrome is associated with hyperleptinemia.

PATHOGENESIS[34]

Psoriasis, whether a disease of the skin or immune system, has been a matter of debate for several years. Cells playing a major role in pathogenesis are.,

a) Keratinocytes
b) T cells
c) Antigen Presenting cells
d) Langerhans cells
e) Natural Killer cells
f) Macrophages
g) Th1 cytokines
h) Growth factors - Vascular Endothelial Growth Factor, Keratinocytegrowth factor.

Factors playing key role in the pathogenesis are.,[34]

i. T cell activation
ii. Hyperproliferation of keratinocytes
iii. Angiogenesis
iv. Cytokine Mediation.

T cell Activation[35-38]

When an injury, either physical or chemical happens, there occurs a complex response involving a major interplay between cytokines and keratinocytes. The defective keratinocytes activates the synthesis and release of cytokines resulting in antigen dependent activation of T- cells. This leads to release of additional cytokines which will stimulate and in turn lead to hyperproliferation of keratinocytes[35,36]. Chang et al demonstrated that cytokines derived from psoriatic lesions potentiate T-lymphocyte activation to a greater extent than those derived from normal human epidermal cells[37]. Moreover only those psoriatic keratinocytes respond well to T-cell supernatants than do normal keratinocytes because they contain specific receptors or signal transducing mechanisms[38].

HYPERPROLIFERATION OF KERATINOCYTES [39,40]

The normal epidermal keratinocytes takes around 26 days for normal maturation and shedding, whereas the psoriatic epidermis takes just 4 days to do the same[39]. Growth factors derived from various cell types are believed to control this hyperproliferation and this forms the basis for many anti-psoriatic drugs of today[40].

ANGIOGENESIS[41-44]

Keratinocytes are a richsource of proangiogenic cytokines like VEGF, IL-8 but the exact mechanism of angiogenesis in psoriasis still remains elusive. The endothelial cells in a developing psoriatic plaque become swollen and shows prominent Golgi apparatus andWeibel-Palade bodies. These cells migrate and lay down a basement membrane with pericytesforming structural support for an interwiningnetwork of blood vessels[43].

This sequence of activation and swelling of endothelial cells leads to widened intercellular spaces and dilatation of dermal capillaries. The capillary loopsin the lesional skin attain a venous morphology with bridged fenestrations. They also express E-selectin, making it easier for leukocyte migration to the skin[44].

Nitric oxide is a heat labile and unstable compound is synthesized in endothelial cells as well as neurons by constitutive NOS synthase (cNOS), while inducible NO synthase (iNOS) is found in leucocytes, macrophages, and mesangial cells. A small amount of NO produced by cNOS in endothelium is responsible for the relaxation of adjacent smooth muscles and prevents adhesion of platelets and leucocytes to the endothelium. This is the anti-inflammatory effect of NO. However, when produced in large

amounts, Nitric oxide can destroy tissues and impair immune response. High levels are demonstrated in immunological disorders like systemic lupus erythematosus or rheumatoid arthritis. Hence, inhibition of iNOS is an effective modality of treatment in these conditions. The production of nitric oxide is approximately 10-fold higher in nonlesional skin of psoriatics and 10-fold higher again in the plaques themselves[44].

CYTOKINE MEDIATORS [45]

Though a complex network of several cytokines are involved in mediating the pathobiology of Psoriasis, none of them seem to be causative. The following table illustrates the key cytokines which play a major role in the pathogenesis of psoriasis.

CYTOKINES IN THE PATHOGENESIS OF PSORIASIS[45-72]	
Cytokine/Growth factor	**Role in Psoriasis**
TNF-α	Stimulates keratinocytes to produce IL-8, ICAM-1, TGF-α, β-defensins, GM-CSF Enhances capacity macrophages to secrete pro-inflammatory cytokines. Stimulates endothelial cells to produce VEGF. Increases keratinocyte proliferation
IFN-γ	Antiproliferative effect on keratinocytes Induces ICAM-1 expression on keratinocytes and endothelial cells

CYTOKINES IN THE PATHOGENESIS OF PSORIASIS[45-72]	
Cytokine/Growth factor	**Role in Psoriasis**
	Influences trafficking of T lymphocytes into lesional epidermis. Stimulation of Antigen Presenting Cell activity Stimulates TNF-α release by phagocytes Upregulates TNF-α receptors
GM-CSF	Induces keratinocyte proliferation Activates neutrophils. Proliferation and migration of endothelial cells
IL-1	Induction of E-selectin and cellular adhesion molecules on keratinocytes Expression of KGF and GM-CSF in fibroblasts. Keratinocyte mitogen mediating angiogenesis
IL-2	Growth factor and chemo-attractant for T cells Inducer of T cell cytotoxicity. Stimulator of NK cell activity.
IL-6	Enhances activation, proliferation and chemotaxis of T-lymphocytes in dermal infiltrate.

CYTOKINES IN THE PATHOGENESIS OF PSORIASIS[45-72]	
Cytokine/Growth factor	**Role in Psoriasis**
	Induces proliferation and activation of B cells and macrophages. Stimulates keratinocyte proliferation.
IL-8	Migration of neutrophils and T-cells in to epidermis Activates and proliferates T-lymphocytes Stimulates angiogenesis
IL-12	Enhances T-cell activation and shunting into Type 1 T cell maturation pathway
Epidermal growth factor family	Increases expression of TGF-α and amphiregulin. Increases EGF/TGF-α receptors in psoriatic epidermis.
Vascular Endothelial Growth Factor	Up-regulation in psoriasis causes erythema. Regulates vascular growth and remodelling VEGF forms a vital link between angiogenesis and cell-mediated inflammation.
Fibroblast growth factor	Mitogenic and Angiogenic properties Present both basally and suprabasally in psoriasis

CYTOKINES IN THE PATHOGENESIS OF PSORIASIS[45-72]	
Cytokine/Growth factor	**Role in Psoriasis**
Neurotrophin growth factor	Stimulates keratinocyte and endothelial cell proliferation Enhances adhesion molecule expression. There is marked up-regulation of NGF receptors, p75 neurotrophin receptor and tyrosine kinase A , in the terminal cutaneous nerves of psoriatic lesions. NGF and substance P contributes to activation of T cells
Endothelin-1	Mitogenic to keratinocytes Chemo-attractant to neutrophils
IL-23	Induces Th-17 cells and activates nuclear STAT-3 transcription.
Th 17	These cells are activated by IL-23 derived from antigen presenting cells(APC's). These Th17 cells in turn produce Th17 cytokines namely IL-17A, IL-17F, IL-22 which bind to the

CYTOKINES IN THE PATHOGENESIS OF PSORIASIS[45-72]	
Cytokine/Growth factor	**Role in Psoriasis**
	respective receptors on stromal cells to promote inflammation by inducing proinflammatory cytokines namely IL-6, IL-8, TNF-α, IL-1β).
IL-22	Acting synergistically with IL-17 it induces defensins, MMPs, S100A7 enhancing keratinocyte mobility. It increases mRNA expression of TNF-α.
IL-17	Enhances surface expression of ICAM-1in fibroblast.

CLINICAL TYPES OF PSORIASIS[73]

CLASSICAL TYPES	Psoriasis vulgaris
	Guttate psoriasis
	Pustular psoriasis
	Psoriatic arthritis
	Erythrodermic psoriasis
SPECIAL TYPES	Elephantine
	Rupioid
	Ostraceous
ATYPICAL FORMS	Follicular
	Linear
	Lichenoid
	Zonal
	Verrucous
	Seborrheic
	Ocular
	Mucosal

LOCALISED	Flexural
	Scalp
	Palms and Soles
	Nail
	Penis

PALMOPLANTAR PSORIASIS[74,75]

It is one of the localized forms of psoriasis which either can occur alone or along with involvement of other areas.

The lesions in most cases are well defined plaques with less scaling with the surface often showing fissures. It can either be pustular or non-pustular.

The following forms of lesions can occur over palms and soles

1. Diffuse hyperkeratotic plaques
2. Erythematous patches and plaques with minute superficial pustules studded over it
3. Discrete scaly patches and plaques
4. Rupioid lesions over soles with characteristic limpet-like scales (rarely).

Palmoplantar psoriasis can also be classified as

1. Pustular - Acute pustularbacterid
   Chronic pustularbacterid
   Palmoplantar psoriasis with pustules
2. Non pustular - Diffuse
   Annular
   Delling or crateriform
   Marginal keratotic

Noble distinguished four clinical variants of palmoplantar psoriasis:

a) Typical red patches sharply demarcated and covered by adherent psoriatic scales.

b) Diffuse mild hyperkeratosis with rhagades and scales

c) Thick hyperkeratotic layer resembling hereditary type of palmoplantarkeratoderma

d) Diffuse erythema

THERAPEUTIC OPTIONS FOR PALMOPLANTAR PSORIASIS

Various therapeutic options are available for palmoplantar psoriasis. These can be divided into topical, physical and systemic modalities

TOPICAL[76]

1. Emollients
2. Salicylic acid
3. Topical corticosteroids
4. Vitamin D analogues
5. Coal tar
6. Dithranol
7. Topical psoralen
8. Topical retinoids (Tazarotene)
9. Topical cytostatic therapy
10. Topical tacrolimus

PHYSICAL[77]

1. Photochemotherapy (PUVA)
2. Narrow band UVB (311nm)
3. Monochromatic excimer light (308nm)

SYSTEMIC [78]

1. Mehotrexate
2. Cyclosporine
3. Acitretin
4. Infliximab
5. Etanercept

In our study we compare the therapeutic efficacy between one from each of these classes namely topical clobetasol and calcipotriol combination, Narrow band UVB as a physical modality and systemic methotrexate.

TOPICAL CORTICOSTEROIDS[79]

Corticosteroids diffuse through the stratum corneum barrier and through cell membranes to reach the cytoplasm of keratinocytes. Diffusion through the stratum corneum is considered to be the rate-limiting step in

delivery of the drug. In the cytoplasm they bind to a specific receptor, the glucocorticoid receptor alpha (GRά). This binding of the receptor to its ligand results in activation of the receptor which dissociates from the other components of the tetrameric complex.

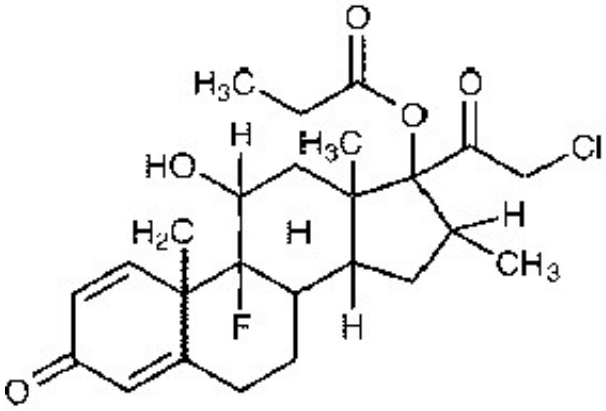
The ligand-bound receptor then enters the nuclear compartment and interacts with specific response elements on the genome, glucocorticoid response elements (GREs). This modulates transcription of numerous genes. In addition the ligand-bound receptor can inhibit, directly or indirectly, the activity of other transcription factors including NFκB, AP-1 and NFAT. These interactions lead to changes in the expression of a wide range of genes, resulting in diverse cellular effects which include suppression of the production of inflammatory cytokines, inhibition of T-cell activation, changes in the function of endothelial cells, granulocytes, mast cells and fibroblasts, and inhibition of proliferation. Part of this anti-inflammatory activity of corticosteroids may be explained by their ability to induce synthesis of lipocortin, a family of glycoproteins which regulate the activity of phospholipase A2. This enzyme affects the production of arachidonic acid, the precursor for leukotrienes and prostaglandins.

Topically applied corticosteroids are of established value in psoriasis. Corticosteroids have the merits of ease of application and removal, lack of irritancy and the absence of staining of skin or linen. Topical steroids under occlusion do have a definite role in managing recalcitrant psoriasis of the scalp, hands, feet and other areas.

CLOBETASOL PROPIONATE[80]

Clobetasol propionate cream is a super potent steroid, which is one of the modalities of treatment of palmo plantar psoriasis. Clobetasol propionate gel, cream and ointment contain the active compound clobetasol propionate, a synthetic corticosteroid. Clobetasol, an analog of prednisolone, has a high degree of glucocorticoid activity and a slight mineralocorticoid activity.

Clobetasol propionate is a white to cream-colored crystalline powder insoluble in water. Chemically, it is 21-chloro-9-fluoro-11β 17-dihydroxy-16β-methylpregna-1, 4-diene-3,20-dione 17-propionate, and it has the following structural formula:

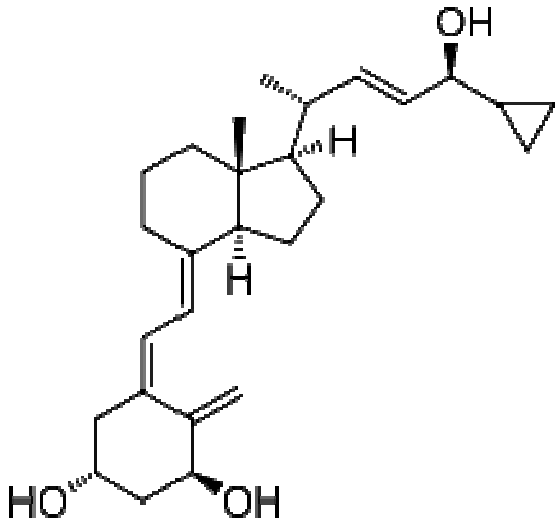


Like other topical corticosteroids, clobetasol propionate has anti inflammatory, anti pruritic, and vasoconstrictive properties. Each gram of the 0.05% ointment contains clobetasol propionate 0.5 mg in a propylene glycol base, sorbitansesquioleate and white petrolatum. Its long-term usage causes hypopigmentation, atrophy, thinning of skin, telangiectasias and tachyphylaxis.

CALCIPOTRIOL[81]

The naturally occurring, active metabolite of vitamin D3, 1,25-dihydroxy vitamin D3 (calcitriol), and three synthetic analogues, calcipotriol, 1,24-dihydroxy vitamin D3 (tacalcitol) and 1,25-dihydroxy vitamin D3 (maxacalcitol), have proven to be effective when applied topically in psoriasis.

Chemically Calcipotriol is (1R,3S,5E)-5-{2-[(1R,3aS,4Z,7aR)-1-[(2R,3E)-5-cyclopropyl- 5-hydroxypent-3-en-2-yl]-7a-methyl-octahydro-1H-inden-4-ylidene] ethylidene} - 4-methylidenecyclohexane-1,3-diol.



The mechanism of action of topical calcipotriol is via vitamin D3 receptor-mediated effects on the proliferation and differentiation of epidermal keratinocytes and on the immunological features of psoriasis, including shifting the Th1 cytokine profile of plaques towards a Th2 cytokine profile.

Vitamin D3 in the formof 1,25- dihydroxy vitamin D3 acts mainly via the Vitamin D3 Receptor to regulate cell growth, differentiation and immune function as well as calcium and phosphorus metabolism. When the

VDR is activated by its ligand or the synthetic analogues like calcipotriol, the drug-receptor complex in association with retinoid X receptor- ά[RXR-ά], binds to specific DNA binding sites called vitamin D3 response elements. Subsequently there is induction or repression of the gene that contains these elements.

Vitamin D3 inhibits proliferation of keratinocytes in culture and modulates epidermal differentiation. It promotes formation of the cornified envelope by increasing gene expression and protein levels of involucrin and transglutaminase. In addition, Vitamin D3 has a number of effects on inflammation. Vitamin D3 inhibits production of IL-2 and IL-6 by T cells, blocks transcription of IFN-γ and GM- CSF and mRNA and inhibits cytotoxic T- cell and natural killer cell activity.

Side effects of calcipotriol include local irritation, hypercalcaemia, photosensitivity and allergic contact dermatitis.

COMBINATION OF CALCIPOTRIOL AND CLOBETASOL PROPIONATE[82]

Palmoplantar psoriasis is characterized by its long term course and variable resistance to treatment. The three main requisites in treating such condition include good patient compliance, efficacious agent and low toxicity profile of the drug.

In a study by Katoh et al, the combination therapy with 0.0003% calcipotriol and 0.05% clobetasol propionate as a premixed ointment was far more efficacious than the monotherapy as it resulted in 50% reduction in the eruption score after 2 weeks, lower eruption score after 6 weeks and less adverse effects.

PHOTOTHERAPY:[84]

The electromagnetic radiation are broadly classified into the following classe:

1. Gamma radiation → < 100 nanometer
2. X-ray radiation → 0.01 to 10 nanometers
3. Ultraviolet radiation A → 320-400 nanometers
4. Ultraviolet radiation B → 280-320 nanometers

5. Ultraviolet radiation C → 100-280 nanometers
6. Visible radiation → 400-700 nanometers
7. Infrared radiation → 700 nanometers-one millimeter
8. Terahertz radiation → one millimeter-100 microns
9. Microwave radiation → 10 millimeter-200millimeter
10. Radio waves → 10 meters-1000 meters

ULTRAVIOLET RADIATION[84]

The wavelength of UV rays is shorter than violet end of the visible spectrum and longer than the X-ray. Ultraviolet light in this very shortest range can ionise atoms changing its physical behavior in a greater way.

At its middle range, UV rays do not ionize but break chemical bonds, making those molecules to be reactive unusually. For example, Sunburn, is found to be caused by disruptive effects of middle range UV radiation on skin cells, which causes skin cancer. UV rays in this range can irreparably damage the complex structure of DNA molecules in these cells producing thymine dimers making it into a very potent mutagen.

The Sun emits significant amount of UV radiation, including extremely short wavelength Ultraviolet light that would potentially destroy

most of the life on earth. Most of these Sun's most-damaging Ultraviolet wavelengths are absorbed by atmosphere and the ozone layer before they reach the earth's surface.

The higher energy ranges of Ultraviolet light are absorbed by nitrogen gas and, at longer wavelengths, absorbed by simple diatomic oxygen in the air. Most of the Ultraviolet light in the mid-range of energy is blocked sufficiently by ozone layer, which absorbs wavelengths in 200–315 nm range, the lower part of which is too long to be absorbed by ordinary oxygen in air.

The very lowest energy range of UV between 315 nm and visible light called the UV-A neither gets blocked by the atmosphere, nor does it cause sunburn and biological damage. However, it is not absolutely harmless and does produce oxygen radicals, mutations and eventually skin damage and cancers.

SKIN PHOTOTYPES[85]

1. Always burns, never tans
2. Burns always, sometimes tans
3. Sometimes burns, always tans
4. Never burns, always tans
5. Moderate amount of pigmentation
6. Deep pigmentation

Detailed history will determine types 1 to 4

Types 5 and 6 can be determined by physical examination

NARROWBAND UV- B IN PSORIASIS[86]

NBUVB is widely used in various dermatological conditions as a novel therapeutic intervention. Fisher was the first person who identified that narrow band ultraviolet B radiation with a wavelength of 313 (311±2) nanometer is efficient in clearing the lesions. Even at higher doses, no notable erythema is;

Jaenicke et al noted better clearance with a wavelength of 313 nanometers[87].

These observations led to the invention of the artificial fluorescent lamps containing phosphorus (TL-01)[87].

In 1988, Van Weeldenet al[88] and Green et al[89]used the florescent lamps in two different studies.

MECHANISM OF ACTION[90,91,92]:

1. The nucleotides of DNA absorb the UVB rays which leads to formation of DNA photoadducts with pyrimidine dimers, thereby interfering with cell cycle progression and causing arrest of growth.
2. UVB facilitates release of prostaglandins which interferes with expression and production of interferon and interleukins.
3. Decreases IL-12, IL-18 IFN-γ and IL-23 expression by inducing their apoptosis.
4. Depletion of T cell and NK cell activity.
5. Suppression of Antigen presenting cell activity.
6. Down regulation of Th 17 cells.

INDICATIONS[93]

1. Psoriasis
2. Atopic Dermatitis
3. Generalised lichen planus
4. Seborrheic dermatitis
5. Mycosis fungoides
6. Prurigonodularis
7. Scleroderma
8. Vitiligo
9. PityriasisRosea
10. Parapsoriasis
11. Pruritus
12. Pityriasisrubrapilaris

CONTRAINDICATIONS[93]

1. History of exposure to Aresenic
2. History of exposure to ionizing radiation
3. History of previous melanoma or multiple non-melanoma skin cancer.
4. Family history of melanoma
5. Type I skin individuals

Hand & Foot Phototherapy chamber

The chamber consists of both UVA and NBUVB lamps with a built in dosimetry which helped to measure the irradiation of the unit continuously.

Technical data:-

1. No. of lamps: 4 UVA & 4 NBUVB lamps
2. Lamp wattage: 100W/6ft each
3. Electronic timer: micro control based
4. Reflector: aluminum (mirror type)
5. Operating voltage: 220V to 230V, 50 Hz

Patients were given protective eye glasses and genitalia were covered.

PROCEDURE[94]:

Based on the Minimum Erythema Dose(MED)**,** initial dose is calculated.

MED is the lowest possible dose of UVB which is able to produce a well defined erythema at the test site.It isusually determined 24 hours after exposure of UVB on back/buttocks around 1cm x 1cm. So initial dose will be 70% of minimal erythema dose.

Minimal erythema dose for skin type 4 is 600 mJ/cm^{2}and for skin type 5 is 1100mJ/cm^2 as determined in a study by Pai et al.

However the latest consensus is the starting dose is determined by the skin type and not by minimal erythema dose

Dose recommendations are as follows[94]:

Skin type	Initial Dose (milli Joules/square centimeter)	Dose increments(milli Joules/square centimeter)
1	130	15
2	220	25
3	260	40
4	330	45
5	350	60
6	400	65

Erythema response is graded as[95]:

a) No erythema

b) Mild erythema –grade 1

c) Moderate and well defined erythema – grade 2

d) Severe painful erythema persisting for > 24 hours –grade 3.

No erythema-Dose is increased by 20 % of last dose[96]

- Grade 1 - Previous dose is maintained and subsequent dose increment is reduced to 10 %.
- Grade 2 - Postpone one treatment, repeat previous dose at next visit and reduce to 10 % increment.
- Grade 3 - No treatment is offered until recovery and further treatment is given by reducing exposure dose by half and 10 % increment thereafter.

If MED is calculated, dose increment should be 10 % of initial MED for the initial 20 exposures and as per physicians discretion thereafter.

Frequency of exposure is thrice or five times per week[97].

If dose is missed, NBUVB can be restarted.

- < 1 week - Maintain the last exposure dose.
- 1-2 weeks - Restart at a dose < 25 % of the last dose.
- 2-3weeks - Restart at 50 % depleted dose.
- >3 weeks - Restart from the previous starting dose.

In India,approach commonly practiced involves a standard starting dose of 280mJ/cm2 followed by stepwise increase of 20% depending on the patient's erythema response[97].

SIDE EFFECTS[98]:

a) Erythema

b) Blistering

c) Pruritis

d) Reactivation of herpes simplex

e) Exposure keratitis and conjunctivitis

f) Tanning

ADVANTAGES OF NB-UVB OVER PUVA THERAPY[98]

1. No need for intake of psoralens. Hence side effects of psoralens can be avoided.
2. Useful in children under 12 years of age, where psoralen is contraindicated.
3. Can be used in pregnancy and lactation, where psoralens are contraindicated.
4. Can be used in elderly or those with poor hepatic or renal function.

5. No eye protection is necessary outside the chamber.
6. Shorter exposure time as compared to PUVA therapy

SYSTEMIC TREATMENT

INDICATIONS[99-103]:

1. Disabling or widespread psoriatic lesions involving more than 20% of the body surface area
2. Pustular psoriasis of the Von Zumbusch type
3. Erythrodermic psoriasis
4. Psoriasis of palms and soles
5. Nail psoriasis
6. Moderate-to-severe psoriatic arthritis not controlled with NSAIDs
7. Lack of adequate clinical response to topical agents and Phototherapy

METHOTREXATE[104-106]

Methotrexate is an anti-folate agent and an anti-metabolite. It was first synthesized in the year 1950 by Indian scientist YellapragadaSubbarao for targeting cancer cells.

Cell cycle specific S –phase inhibitor and thus finds its use as an anti-cancer drug.

Although available since 1948, it was first used in the treatment of psoriasis from the year 1958 but was FDA approved in the year 1971 and was used as a DMARD from the year 1988.

MECHANISM OF ACTION:[106]

1. Competitively and irreversible inhibition of dihydrofolatereductase, preventing the conversion of dihydrofolate to tetrahydrofolate and thus inhibiting DNA synthesis.

2. Competitive and reversible inhibition of thymidylatesynthetase and AICAR (5-aminoimidazole-4-carboxamide ribonucleotide) transformylase

3. AICAR transformylase is involved in purine biosynthesis. It inhibits the metabolism of intracellular adenosine, which is toxic to T-lymphocytes and is potently anti-inflammatory.

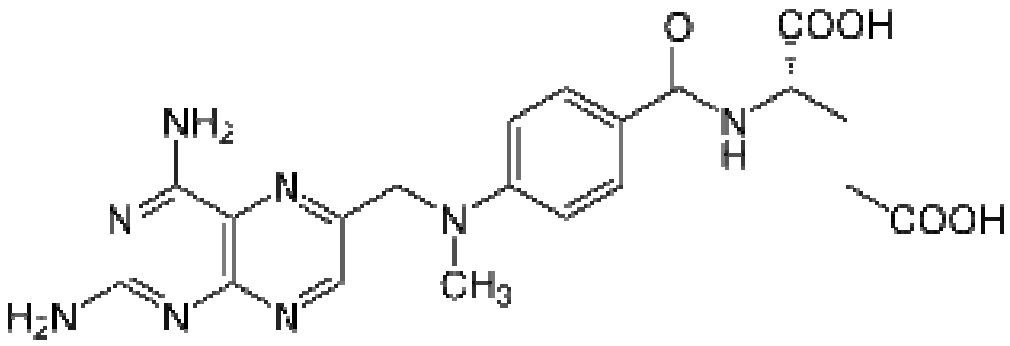
4. It decreases the concentration of S-adenosylmethionine[SAM], a pro-inflammatory mediator by blocking methionine synthetase.

5. It acts as an anti-inflammatory agent, reducing the chemotaxis of the polymorphonuclear cells, inhibiting the C5a induced cutaneous inflammation, reducing the B4-induced chemotaxis and the number of positive OK-T6 cells in the epidermis.

6. It acts as an immunomodulating agent, breaking the production of IL-1 and reducing the density of Langerhans cells in the epidermis, and also appears to have an effect on the antigen-presenting cells.

PHARMACOLOGY[107-110]

CHEMICAL STRUCTURE



After oral administration, it is absorbed quickly and reaches peak serum levels in one or two hours. After intramuscular injection, peak serum levels are detected within half of this time. Dairy foods and non-absorbable antibiotics, such as Neomycin, can reduce its bioavailability.

Methotrexate diffuses and accumulates in the red globules. 50% of the drug binds reversibly to albumin, which means that the concomitant use of other medicines that also bind to proteins can increase its hematological toxicity.

Once absorbed, the levels of Methotrexate in the plasma have a tri-phasic reduction

1. Rapid distribution phase
2. Renal excretion phase
3. Phase of terminal half-life

Route of elimination: 50 to 90% of methotrexate is eliminated through renal pathway by glomerular filtration and to a lesser extent, by tubular secretion. This is reduced in the presence of nonsteroidal anti-inflammatory drugs and sulfonamides.

Being a weak organic acid, it is excreted predominantly by the kidney, the concomitant use of other weak organic acids should be avoided such as salicylates and probenecidthat reduce the renal tubular transport and can prolong the excretion of Methotrexate.

Methotrexate has an age-dependent pharmacokinetic profile, with greater distribution and elimination of the drug in the young. Care must be exercised in older patients, due to a possible reduction in renal function.

Drugs that may increase the potential for methotrexate toxicity include salicylates, nonsteroidal anti-inflammatory drugs, sulfonamides, tetracyclines, chloramphenicol, phenytoin and phenothiazines.

If the patient has normal liver chemistry values, a normal history, and normal physical examination findings, and no risk factors, a liver biopsy is recommended after a cumulative dosage of - 1.5 gm to 2.0 gm for low risk patients.

- 1 gm for higher risk patients.
- Every 6 months for patients with grade IIIA liver biopsy changes

Classification of liver biopsy findings :

Grade 1 : Normal : Fatty infiltration, mild; nuclear variability, mild; portalinflammation, mild.

Grade 2 : Fatty infiltration, moderate to severe; nuclear variability, moderate to severe; portal tract inflammation and necrosis, moderate to severe.

Grade 3 : A : Fibrosis, mild

B : Fibrosis, moderate to severe

Grade 4 : Cirrhosis.

Two methods have been developed that might reduce the need for routine biopsies :

a) Dynamic hepatic scintigraphy
b) Measurement of the serum aminoterminalpropeptide of type III procollagen (PIIINP).

Monitoring for methotrexate therapy :

The drug is excreted largely by the kidneys but there is extensiveenterohepatic cycling. The drug is 50-70% bound to plasma albumin. Beforetreatment, renal, hepatic and marrow function tests must be

normal. Urine should befree of albumin and casts. Toxic effects on the bone marrow include leucopenia,thrombocytopenia, folate deficient megaloblasticanaemia.

Premethotrexate evaluation includes :

Examination :

1) Careful history and physical examination
2) Identification of persons at increased risk for toxicity
3) Recording concomitant medication that may interact with methotrexate.

Blood :

- Haemoglobin percentage
- Total W.B.C. count
- Differential count
- Platelet count

Liver function tests :

- SGOT (serum glutamate oxaloacetic transaminase)
- SGPT (serum glutamate pyruvic transaminase)
- Serum alkaline phosphatase
- S.bilirubin
- S.albumin

Renal function tests :

- Blood urea
- S.creatinine

Urine :

- Sugar, albumin and cast
- Chest radiograph

During Therapy :

1) Leucocyte count, differential count and platelet count (every week for 4 weeks, 1 week after the last dose).
2) Every 3-4 months, 1 week after the last dose
    - Haemoglobin estimation
    - Platelet count
    - Liver function tests

      (SGOT, SGPT, S.alkaline, phosphatase, S.albumin)
    - S.creatinine, blood urea
    - Urine analysis

INDICATIONS[110]

FDA APPROVED

1. Psoriasis
2. Mycosis fungoides[cutaneous T-cell lymphoma]

OFF LABEL USES

1. Atopic dermatitis
2. Behçet's disease
3. Bullous pemphigoid
4. Cutaneous PAN
5. Dermatitis herpetiformis
6. Dermatomyositis
7. IgA pemphigus
8. Leukocytoclasticvasculitis
9. Lupus erythematosus
10. Lymphomatoidpapulosis
11. Morphea
12. Pemphigus foliaceus
13. Pemphigus vulgaris
14. Pityriasislichenoides et varioliformisacuta

15. Pityriasisrubrapilaris
16. Pyodermagangrenosum
17. Reiter's disease
18. Rheumatoid arthritis
19. Sarcoidosis
20. Scleroderma

SIDE EFFECTS

METHOTREXATE IN PSORIASIS[111, 112]

Methotrexate is an immunosuppressive agent which blocks DNA synthesis by inhibiting dihydrofolatereductase. It is typically given either as a single weekly dose of 7.5 to 25 mg per week or divided into three doses each week at 12-hour intervals, Weinstein & Frost, 1971.

Methotrexate is most commonly given via the oral route, however subcutaneous administration is also an option, Zackheim, 1992. Advantages of subcutaneous injections include less nausea and increased bioavailability. Patients may also be more familiar with self-injection because of the proliferation of that administration route with biologic therapy.

In addition to nausea, methotrexate can cause anemia and rarely pancytopenia. Both of these side effects can be reduced with folic acid supplementation as suggested by Duhra et al and Ortiz et al. It was previously thought that folic acid supplementation may reduce the efficacy of methotrexate, but a recent review refutes by Salim et al and Strober et al refutes that claim.

Gilbert et al showed that patients on long-term methotrexate therapy also may develop cirrhosis. Risk factors for this include pre-existing liver disease, alcohol use, diabetes, and obesity as proposed by Langman et al. Though literatures in rheumatology show relatively little mention of screening for cirrhosis, this issue has to be viewed with so much concern and controversy by dermatologists.

Current American Academy of Dermatology (AAD) guidelines suggest a liver biopsy after each cumulative methotrexate dose of 1.5 g; however, studies by Aithal et al and Langman et al suggest that the first liver biopsy may not be necessary in patients without risk factors until 3.5 to 4 g of methotrexate have been given.

Other tests of liver function have been investigated in an attempt to decrease the need for liver biopsies. Maurice et al in 2005 suggest that liver biopsies can be avoided if PIIINP (procollagen III) levels are consistently normal. Another study by Chalmers et al in 2005 showed a seven-fold decrease in biopsies using a PIIINP protocol compared to AAD guidelines.

Based on expert experience, the starting dose of MTX is between 5 and 10 mg/week for the first week. Fast dose escalation is recommended in order to obtain a therapeutic target dose of 15–25 mg/week. The maximum recommended dose is 25 mg/week. A folic acid supplement is necessary. The initiation of treatment by oral administration is preferred. In cases where inadequate response is obtained or in the event of poor gastrointestinal tolerance, subcutaneous dosing can be proposed at the same dose. Published data do not confirm the incidence of hepatic fibrosis. Type 2 diabetes and obesity appear to be significant risk factors in fibrosis. A combination of FibroTests and fibroscans together with measurement of the type III serum procollagenaminopeptide seem to be ideal method for monitoring liver toxicity.

Aims & Objectives

AIM OF THE STUDY

Aim of the study is to study

1) To compare the therapeutic efficacy of

   A) Oral Methotrexate

   B) Hand &Foot Phototherapy using Narrowband UV-B

   C) Topical Calcitriol Plus Clobetasol Propionate Ointment

2) To do Clinical evaluation using PASI scoring and assessing patient's feeling of improvement using DLQI.

Materials & Methods

MATERIALS AND METHODS

For the present study, sixty clinically diagnosed cases of palmoplantar psoriasis were randomly selected from the patients attending out-patient clinic in Department of Dermatology, Rajiv Gandhi Government General Hospital,Chennai from September 2013 to August 2014.

The diagnosis was based upon the clinical history and morphology of lesions. Doubtful cases were subjected to skin biopsy.

STUDYDESIGN : Prospective study

SUBJECTSELECTION

InclusionCriteria:

Subjects of both sexes irrespective of their age having Palmoplantar Psoriasis

ExclusionCriteria:

1. Patients having acute uncontrolled bacterial, viral or fungal infection
2. Patients with impaired renal function or pre-existing renal disease
3. Patients on concomitant hepatotoxic or nephrotoxic drugs for any other long standing illness
4. Pregnant or breastfeeding females
5. Concurrent immunodeficiency state
6. Patients having hepatitis, active or recent
7. Patients having severe anemia, leukopenia or thrombocytopenia
8. Photosensitive dermatoses or history of photo damage
9. Previous or family history of malignant melanoma
10. History of exposure to ionizing radiation
11. Patients with hypersensitivity disorders
12. Patients with hypercalcemia

All these patients were explained about the nature and course of the disease, benefits & possible side effects of treatment. Informed written consent were obtained from all these patients before initiation of treatment.

All the patients will be evaluated as follows

1) History
2) General examination
3) Systemic examination
4) Dermatological examination
5) Investigations
    a) Complete hemogram
    b) Urine analysis
    c) Renal function tests
    d) Liver function tests
    e) Serum calcium, uric acid
    f) Blood VDRL
    g) Elisa for HIV
    h) Chest X-Ray
6) Skin Biopsy in doubtful cases.
7) Opinion regarding evidence of focal sepsis from ENT & Dental departments

TREATMENT PROTOCOL AND METHODOLOGY

Sixty patients with palmoplantar psoriasis were randomly allocated to any of the three following groups.

- Group A : Topical therapy using Calcitriol and Clobetasol Ointment
- Group B : Physical therapy in the form of Hand and Foot phototherapy usingNB-UVB
- Group C : Systemic therapy with oral methotrexate.

GROUP A : SYSTEMIC TREATMENT USING TABLET METHOTREXATE

20 patients were included in this group.

After preliminary investigations, patients were given test dose of 5 mg of Tablet Methotrexate, 2.5 mg to be taken 12 hours apart.

After one week, blood investigations were repeated to look for acute myelosuppression and elevation of liver enzymes.

If the blood investigations were found to be normal, Patients were given Tablet Methotrexate 2.5 mg tablet three tablets a week with a total dosage of 7.5 mg per week according to Weinstein-Frost regimen.

Patients were instructed to take the tablet after food in three divided doses on two consecutive days with a gap of 12 hours in between.

Patients were followed up every 2 weeks for assessment of clinical response and blood investigations. Chest X-ray was repeated at the end of 3 months

GROUP B : HAND AND FOOT PHOTOTHERAPY USING NARROW BAND UV-B

- 20 patients were included in this group
- Patients were made to sit comfortably in a chair with both the hands placed over the upper cubicle and the soles over the lower cubicle
- The patients were advised to wear UV goggles

- Protection to the genitalia was not advised as the light rays are inclined at an angle away from it and protected well by clothing
- Initial UV B dose of 0.25 J was started in all patients
- Patients were instructed to get up from the chair once when the alarm starts beeping
- If the initial dose was tolerated, 20% incremental dose was given at each subsequent visit depending on the patient's erythema response.
- Treatment was given thrice weekly on non-consecutive days.
- Patients were monitored regularly every two weeks.
- Patients were instructed to report immediately if any of the adverse effects were noted.

GROUP C : TOPICAL THERAPY

- 20 patients were included in this group
- Patients were given free samples of an ointment containing a combination of Clobetasol propionate 0.05% w/w with Calcitriol (Vitamin D analogue) 0.0003% w/w ointment.

- The patients were advised to apply the ointment twice daily after application of emollient like liquid paraffin oil.

- The amount of ointment to be applied was based on calculation of fingertip unit i.e., one fingertip unit for each hand and two fingertip units for each sole.

- Patients were strictly advised not to apply the ointment over normal skin but only over the lesional skin

- Patients were advised not to wash off or wipe away the ointment for atleast a period of 30 minutes

- Patients were monitored regularly every two weeks for signs of clinical improvement

- Patients were advised to report immediately if they observed any pain or burning sensation over the lesions.

FOLLOW UP

Patients were reviewed every 4 weeks at intervals of 0,4,8,12,16 weeks for complaints and assessing clinical improvement. These were compared and statistically analysed.

EFFICACY ASSESSMENT

Severity and extent of psoriasis were evaluated using “Psoriasis Area and Severity Index (PASI) score.

Quality of clinical improvement was assessed by Dermatology Life Quality index (DLQI).

Severity of Erythema (E), Desquamation (D) and Induration (I) was recorded on a 5 point scale as follows.

0	Nil
1	Mild
2	Moderate
3	Severe
4	Very severe

The area of involvement was recorded on a 7 point scale as follows

0	Nil
1	<10%
2	10-29%
3	30-49%
4	50-69%
5	70-89%
6	90-100%

PASI was calculated as follows

PASI = Correction factor X Total score X Area of involvement

= 0.2 X (E_U+I_U+D_U)X AU+0.4 X (E_L+I_L+D_L) X AL

A - Area

U - Upper limb

L - Lower limb.

Observations & Results

OBSERVATION AND RESULTS

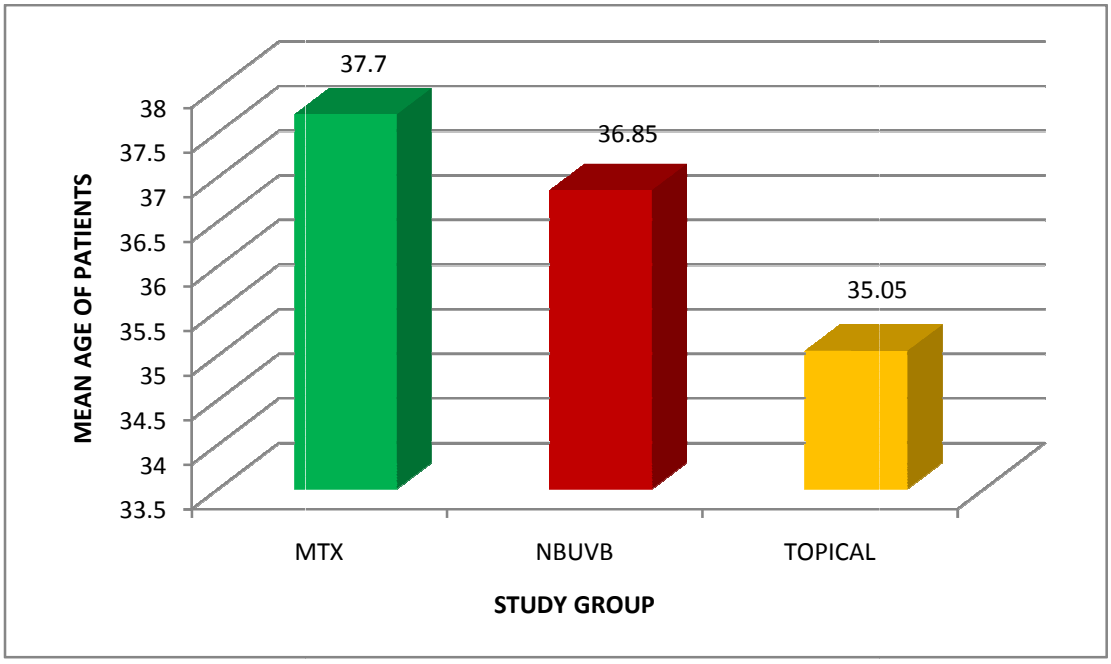
AGE DISTRIBUTION

The mean age in our study group was 37.70 years in Methotrexate, 36.85 years in NBUVB group and 35.05 years in Topical Ointmentgroup. The minimum age in Methotrexate, NBUVB and Topical Ointment is 22, 20, 12 years respectively. The maximum age in Methotrexate, NBUVB and Topical Ointment is 56, 56, 48 years respectively.

Table -1 :Showing age distribution

Age	N	Mean	Std. Dev	Median	Minimum	Maximum
MTX	20	37.70	8.82	37.00	22	56
NBUVB	20	36.85	10.93	36.00	20	56
TOPICAL	20	35.05	8.75	36.50	12	48

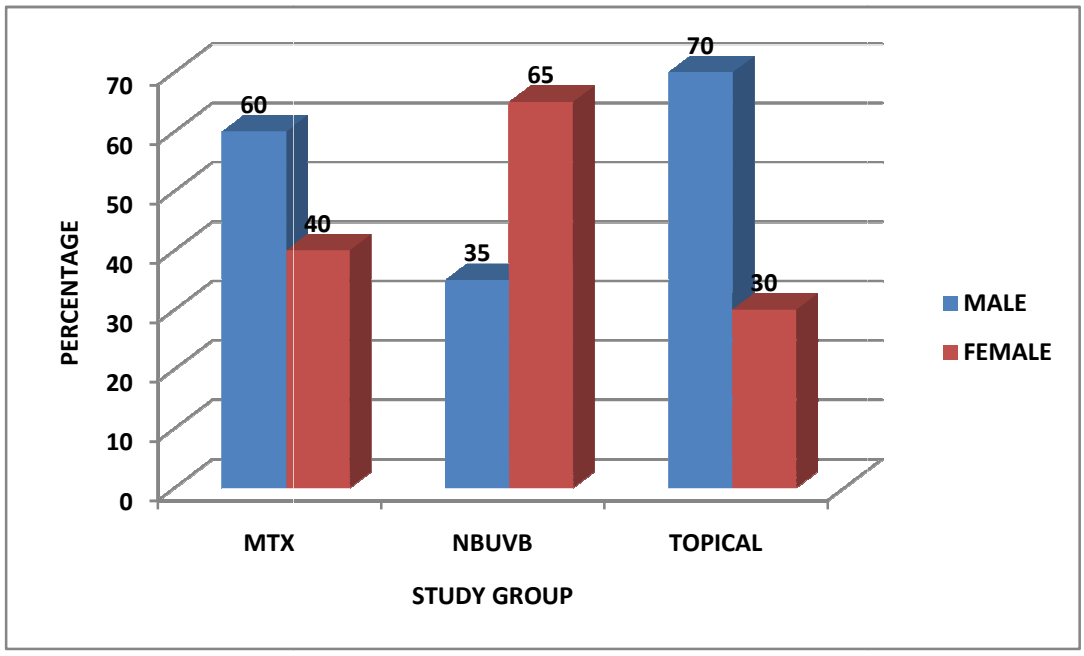
Figure 1 :showing mean age of patients in three groups



SEX DISTRIBUTION

Males were relatively more in our study when compared to females.

Figure 2- showing Sex distribution

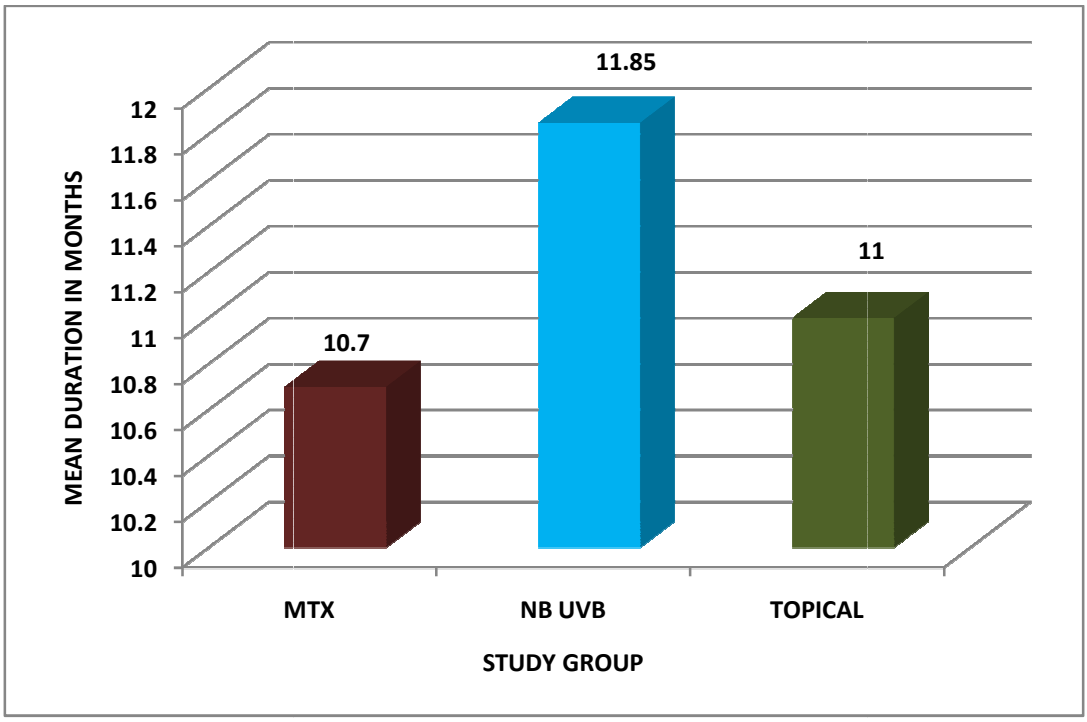


In Methotrexate group 60 % were males, 40% were females. In NBUVB group 35 % were males, 65% were females and Topical group 70 % were males, 30 % were females.

DURATION OF ILLNESS

The duration of illness varied in three groups. In Methotrexate group Duration of illness varied from 1 month to 30 months. In NBUVB group duration varied from 2 months to 30 months. In TOPICAL group duration of illness varied from 3 months to 26 months.

Figure 3 : showing duration of illness in three groups



The mean duration in Methotrexate group is 10.7 months, NBUVB group is 11.85 months, and Topical group is 11months.

Table 3 :Showing duration of illness in three groups

Duration (months)	N	Mean	Std. Dev	Median	Minimum	Maximum
METHOTREXATE	20	10.7	8.16	8.5	1	30
NB UVB	20	11.85	8.48	10.00	2	30
TOPICAL	20	11	6.42	9.50	3	26

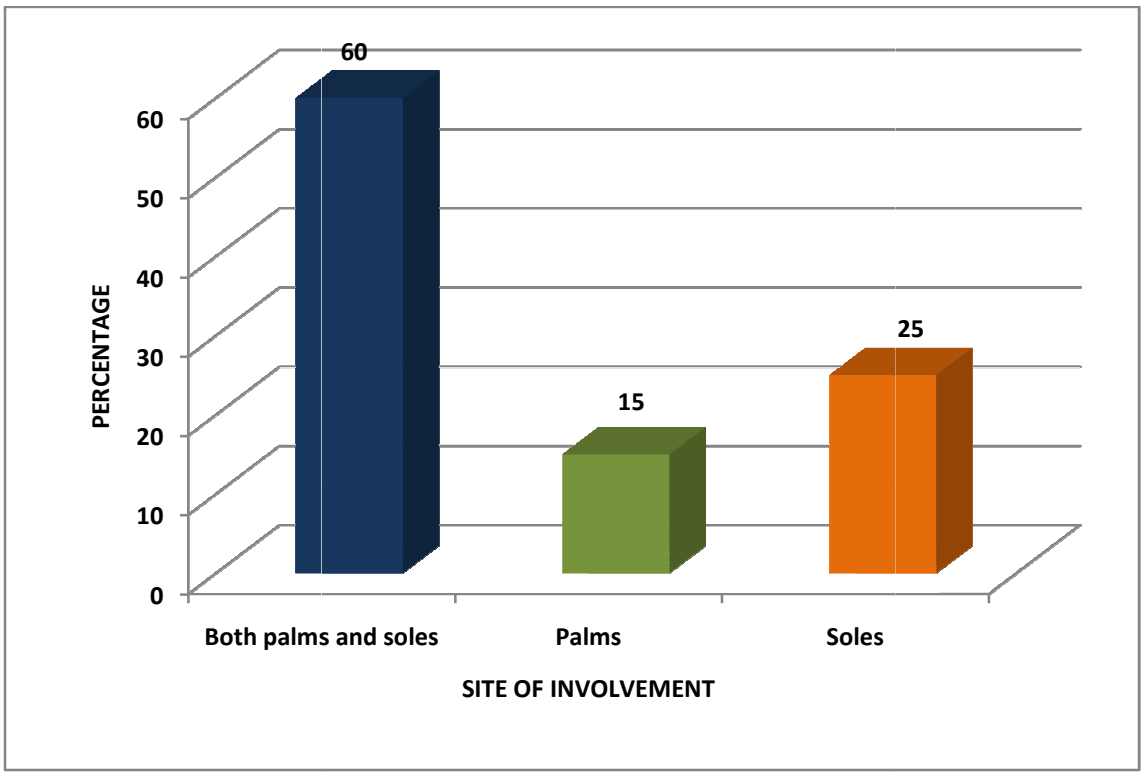
Sites involved

Of the cases studied the site of involvement was both palms and soles in 36 (60.%) cases, whereas only palms was involved in 9 (15%) cases and only soles involved in 15 (25%) cases.

Table 4 : Site of involvement of Palmoplantar Psoriasis cases

SITE OF INVOLVEMENT	NUMBER	PERCENT
Both palms and soles	36	60
Palms	09	15
Soles	15	25
Total	60	100

Figure 4 :Site of involvement of Palmoplantar psoriasis cases



In Group 1, the sites involved were both palm1s and soles in 14 (70%) cases, only soles in 4 (20%) cases and only palms in 2 (20%) cases.

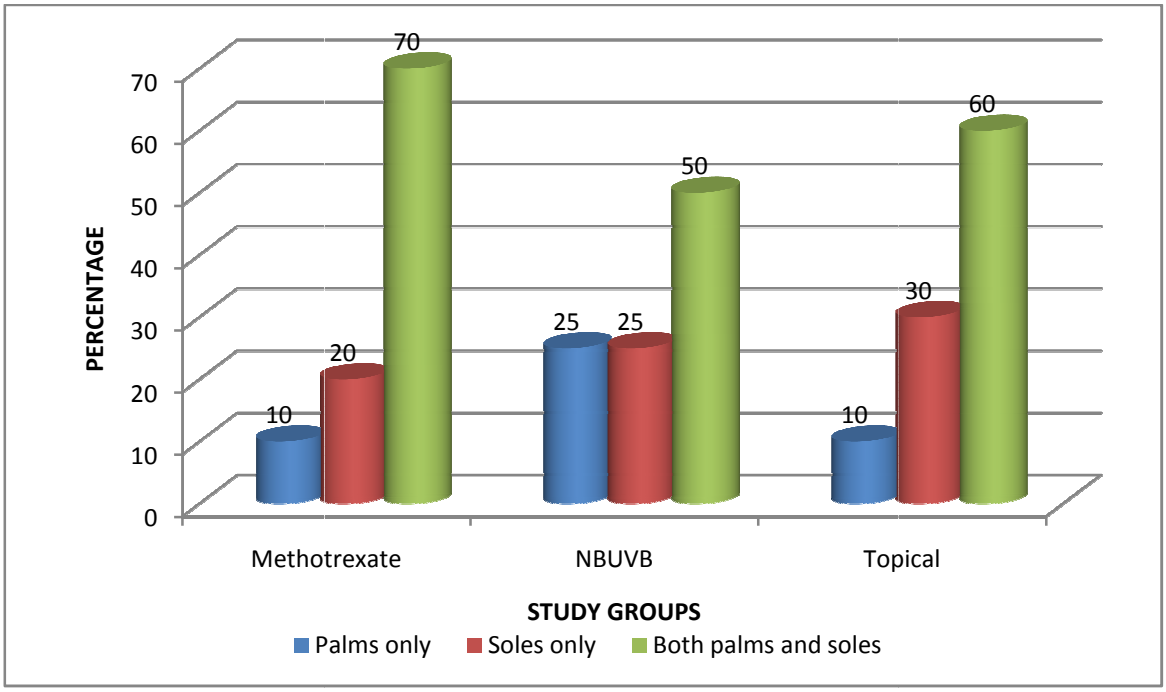
In Group 2, the sites involved were both palms and soles in 10 (50%) cases, only soles in 5 (25%) cases and only palms in 5 (25%) cases.

In Group 3, the sites involved were both palms and soles in 12 (60%) cases, only soles in 6 (30%) cases and only palms in 2 (10%) cases.

Table 5 :Site of involvement in different treatment groups

Site	Methotrexate		NBUVB		Topical	
	Number	Percent	Number	Percent	Number	Percent
Palms only	2	10	5	25	2	10
Soles only	4	20	5	25	6	30
Both palms and soles	14	70	10	50	12	60
Total	20	100	20	100	20	100

Figure 5 : Site of involvement in different treatment groups



NAIL CHANGES

Nail changes were present in 29 of our patients, 11 in Methotrexate group, 7 in NB UVB group and 11 in Topical group.

The commonly noted nail changes were Pitting, Onycholysis,Subungual hyperkeratosis and Ridging. More than one morphological nail changes were present in a single patient.

In Methotrexate group

Four patients had pitting, threepatients had onycholysis, threepatientshad subungual hyperkeratosis,one patienthad ridging.

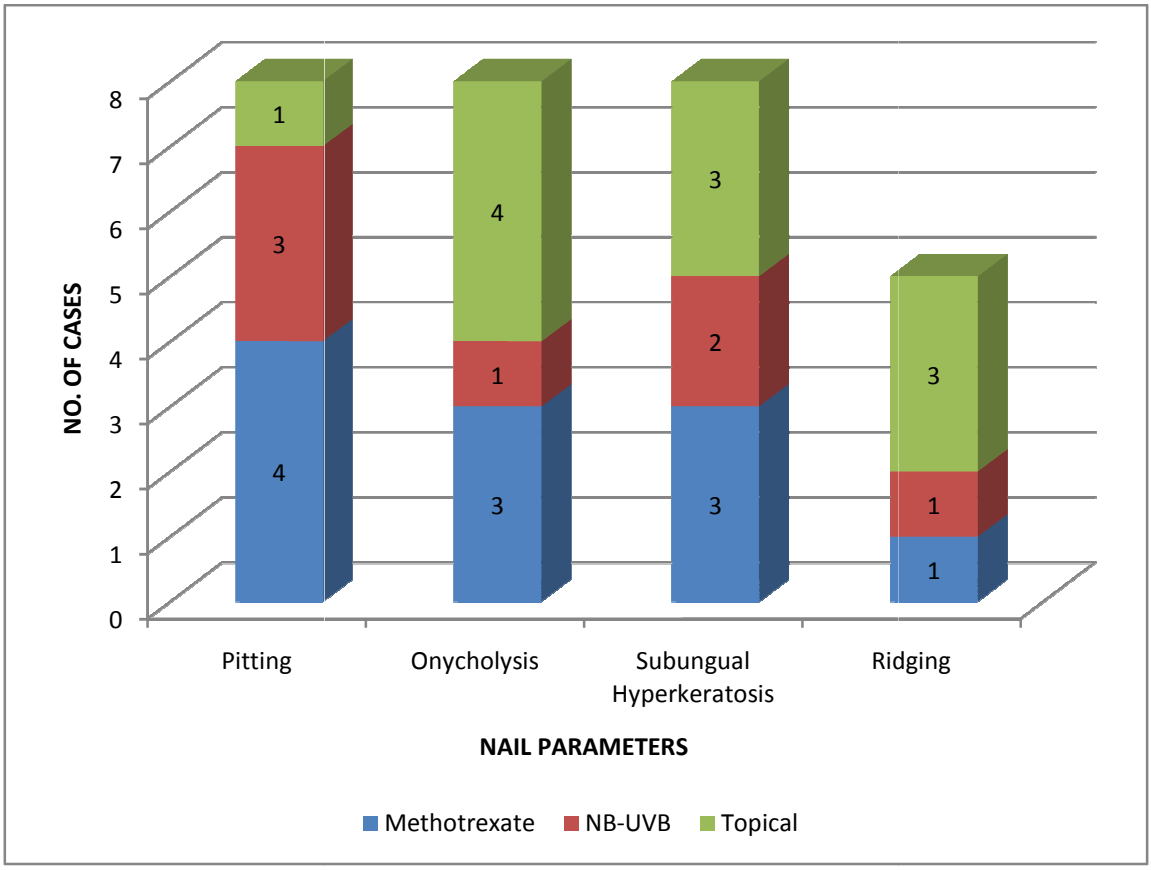
In NBUVB group

Three patients had pitting,one patient had onycholysis,two patientshad subungual hyperkeratosis,one patienthad ridging.

In Topical group

One patient had pitting,fourpatients had onycholysis,three patientshad subungual hyperkeratosis,three patientshad ridging.

Figure 6 :Showing nail changes in three groups



Eight patients had pitting, eight patients had onycholysis, eight patients had subungual hyperkeratosis and five patients had ridging out of twenty nine patients with nail involvement in all three groups of our study.

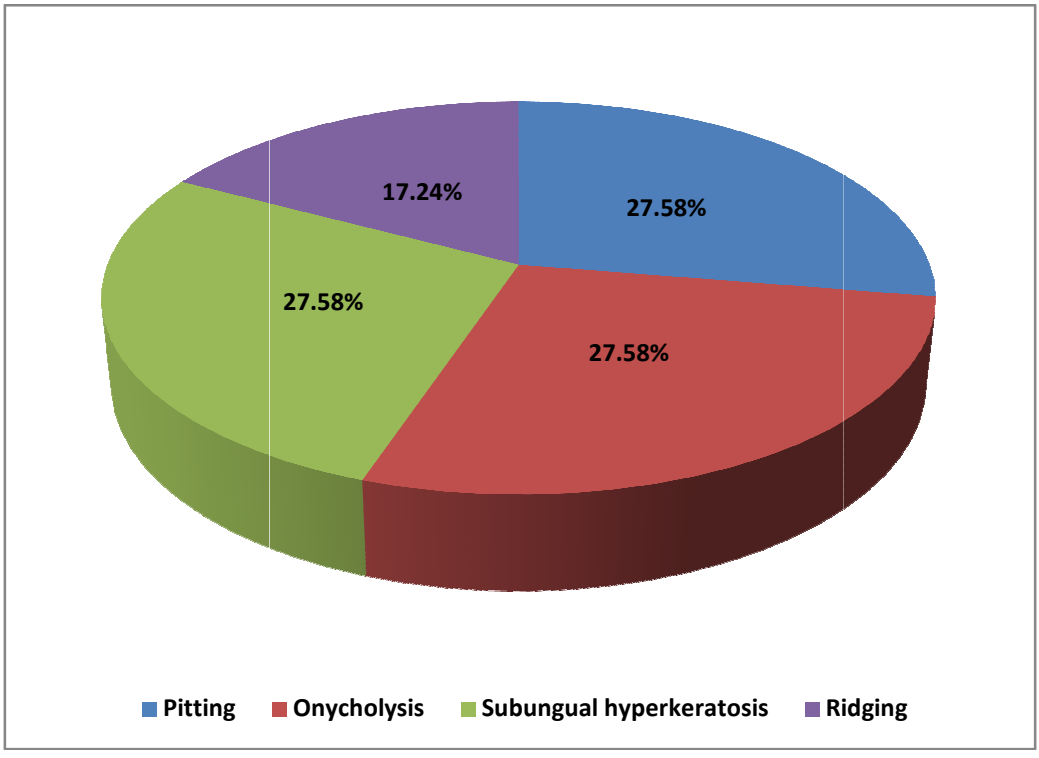
Table 6 :Showing nail involvement in three groups

Group	Nail Involvement				Total
	Pitting	Onycholysis	Subungual Hyperkeratosis	Ridging	
Methotrexate	4	3	3	1	11
NB-UVB	3	1	2	1	7
Topical	1	4	3	3	11
Total	8	8	8	5	29

Table 7 :Showing percentage of nail involvement in three groups

Nail finding	Percentage
Pitting	27.58%
Onycholysis	27.58%
Subungual hyperkeratosis	27.58%
Ridging	17.24%

Figure 7 : Showing percentage of nail involvement in three groups



OTHER SITES

No patients had mucous membrane, scalp, joint involvement.

PASI REDUCTION

The following tables shows the mean PASI score at baseline and reduction of mean PASI score at 4 weeks, 8 weeks, 12 weeks, 16 weeks in PUVA, NBUVB, PUVASOL groups.

The mean PASI score at baseline (Table 8) was 30.98 in Methotrexate group, 28.19 in NBUVB group, and 26.66 in TOPICAL group. The minimum mean PASI score at baseline in Methotrexate, NBUVB and Topical group is 20.0, 22.4 and 19.2 respectively. The maximum mean PASI score at baseline in PUVA, NBUVB and PUVASOL group is 39.4, 36.8 and 32.8 respectively.

Table 8:Showing mean PASI score at baseline in three groups

PASI 0	N	Mean	Std. Dev	Median	Minimum	Maximum
MTX	20	30.98	5.32	31.29	20.0	39.4
NBUVB	20	28.19	4.21	28.10	22.4	36.8
TOPICAL	20	26.66	3.99	26.90	19.2	32.8

The mean PASI score at 4 weeks (Table 9) was 16.34 in Methotrexate group, 17.19 in NBUVB group, and 14.91 in TOPICAL group.

The minimum mean PASI score at 4 weeks in PUVA, NBUVB and PUVASOL group is 10.2, 12.0, and 10.0 respectively. The maximum mean PASI score at 4 weeks in PUVA, NBUVB and PUVASOL group is 22.2, 22.8 and 20.2 respectively.

Table 9 :Showing mean PASI score at 4 weeks in three groups

PASI 4	N	Mean	Std. Dev	Median	Minimum	Maximum
MTX	20	16.34	2.85	16.10	10.2	22.2
NBUVB	20	17.19	3.23	17.80	12.0	22.8
TOPICAL	20	14.91	2.17	15.0	10.0	20.2

The mean PASI score at 8 weeks (Table 10) was 10.12 in Methotrexate group, 11.42 in NBUVB group, and 12.04 in Topical group.

The minimum mean PASI score at 8 weeks in Methotrexate, NBUVB and Topical group is 4.4, 6.4, and 5.6 respectively. The maximum mean PASI score at 8 weeks in Methotrexate, NBUVB and Topical group is 13.4, 18.4 and 13.4 respectively.

Table 10 :Showing mean PASI score at 8 weeks in three groups

PASI 8	N	Mean	Std. Dev	Median	Minimum	Maximum
MTX	18	10.12	3.95	10.40	4.4	13.4
NBUVB	19	11.42	3.49	11.10	6.4	18.4
TOPICAL	18	12.04	2.13	12.25	5.6	13.4

The mean PASI score at 12 weeks (Table 10) was 3.40 in Methotrexate group, 5.20 in NBUVB group, and 5.60 in Topical group.

The minimum mean PASI score at 12 weeks in Methotrexate, NBUVB and Topical group is 0.0, 0.0 and 2.2 respectively. The maximum mean PASI score at 12 weeks in Methotrexate, NBUVB and Topical group is 7.6, 7.2 and 7.8 respectively.

Table 11 :Showing mean PASI score at 12 weeks in three groups

PASI 12	N	Mean	Std. Dev	Median	Minimum	Maximum
MTX	20	3.40	2.23	3.15	0.0	7.60
NBUVB	13	5.40	3.61	5.60	0.0	7.20
TOPICAL	20	5.60	2.81	5.80	2.2	7.80

The mean PASI score at 16 weeks (Table 11) was 0.49 in Methotrexate group, 1.76 in NBUVB group, and 1.45 in TOPICAL group. The minimum mean PASI score at 16 weeks is 0.0 in all three groups. The maximum mean PASI score at 16 weeks in Methotrexate, NBUVB and Topical group is 3.2, 3.4 and 4.2 respectively.

Table 12 :Showing mean PASI score at 16 weeks in three groups

PASI 16	N	Mean	Std. Dev	Median	Minimum	Maximum
MTX	19	0.49	0.81	0.00	0.0	3.2
NBUVB	13	1.76	1.51	0.00	0.0	3.4
TOPICAL	20	1.45	2.20	3.60	0.0	4.2

From tables 8-12 we inferred that there was gradual reduction in PASI score in all three groups.

Table 13 :Shows mean reduction in PASI score among three groups

Duration	Mean PASI score		
	MTX	NBUVB	TOPICAL
Baseline	30.98	28.19	28.66
4 weeks	16.34	17.19	14.91
8weeks	10.12	11.42	12.04
12 weeks	3.40	5.40	5.60
16 weeks	0.49	1.76	1.45

In Methotrexate group the mean PASI score at baseline is 30.98 and it was reduced to 0.49 at 16 weeks.

In NBUVB group the mean PASI score while enrolling in study was 28.19 where as it was reduced to 1.76 at 16 weeks.

In Topical group the mean PASI score was 28.66 at baseline and it was reduced to 1.45 at 16 weeks of Topical therapy.

Therefore the mean reduction of PASI score at 16 weeks is more in Methotrexate group, followed by Topical group. NBUVB has lesser reduction in mean PASI score among three groups.

Figure 8: Showing mean reduction in PASI scores

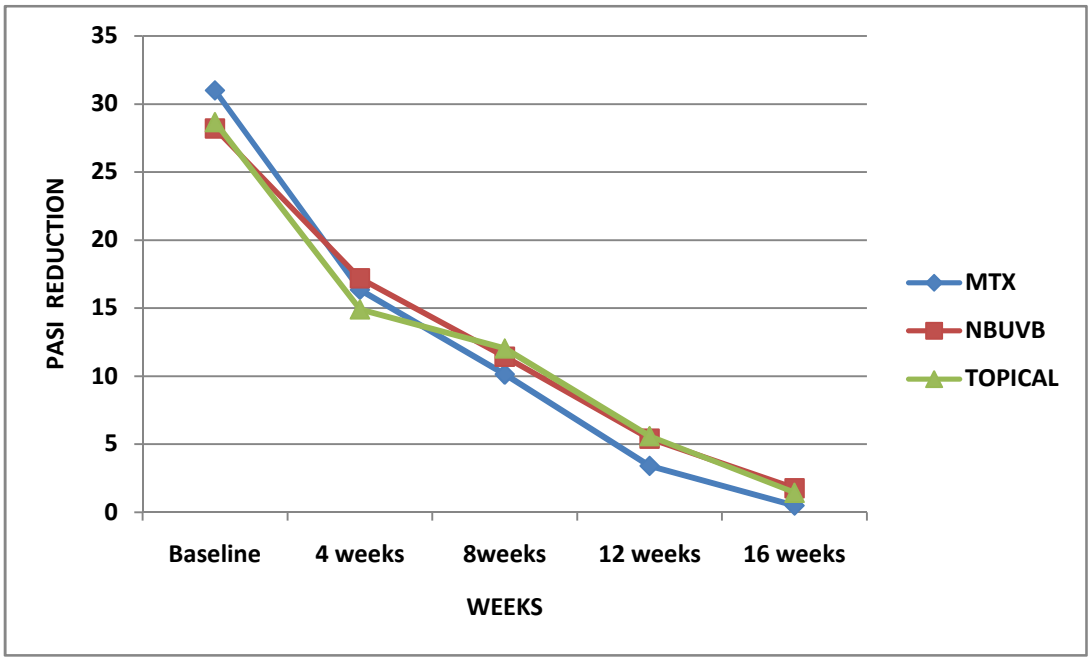


Table 14 shows P values by comparing three groups with one another. There was no statistically significant reduction in PASI score at 0, 4, 8, 12 and 16 weeks when MTX and NBUVB are compared.

When MTX and TOPICAL groups are compared there is no statistically difference in reduction in PASI score at 0, 4, 8 weeks. But at 12 and 16 weeks there is statistically significant ($P<0.001$) reduction in PASI score.

Table 14 :Shows P values of PASI Score reduction when twogroups are compared

Variables	P-Values		
	MTXvs NBUVB	**NBUVBvsTOPICAL**	**MTXvsTOPICAL**
PASI 0	0.579	0.903	0.695
PASI 4	0.933	0.255	0.184
PASI 8	0.627	0.024	0.101
PASI 12	0.150	0.001	0.035
PASI 16	0.694	0.001	0.001

When NBUVB and TOPICAL groups were compared there was no statistically significant difference in PASI score at 0, 4, 8, 12 weeks. However at 16 weeks there is statistically significant PASI reduction ($P<0.001$).

PERCENTAGE REDUCTION OF PASI SCORE

Table 15 :Showing percentage mean reduction in PASI score in three groups

Duration	MTX	NBUVB	TOPICAL
Baseline	0	0	0
4 weeks	36.2	30.99	31.89
8 weeks	67.5	59.2	64.94
12 weeks	91.0	72.0	80.53
16 Weeks	98.9	82.9	86.44

The above table shows that there is gradual increase in percentage mean reduction of PASI score over weeks. When compared to baseline mean PASI score there was 98.9 % reduction in mean PASI score at 16 weeks in MTX group and 82.9% reduction in mean PASI score at 16 weeks in NBUVB group. In TOPICAL group there is 86.44% reduction in mean PASI score at 16 weeks.

MTX group has the maximum percentage reduction in mean PASI score at 16 weeks, followed by TOPICAL group. NBUVB shows least reduction when all three groups are compared.

RESPONSE TO THERAPY

Based on percentage reduction in PASI score the results were graded as excellent (100%), good (75-100%), moderate (50- 75%) and poor (< 50%).

RESPONSE TO THERAPY IN METHOTREXATE GROUP

In Methotrexate group out of 20 patients 15 patients had complete clearance at 16 weeks and 4 had good response. 1 patient discontinued treatment at 16 weeks of therapy due to intolerance to drug.

Table 16:Response to treatment in Methotrexate group

Results	No. of patients	Percentage	% reduction in PASI score at 16 weeks
Excellent	15	75.00	100
Good	4	20.00	75-100
Moderate	-	-	50-75
Poor response	-	-	<50
Discontinued	1	5.00	-

Therefore in Methotrexate group 75.00% of patients had excellent response and 20.00 % of patients had good response at 16 weeks.

RESPONSE TO THERAPY IN NBUVB GROUP

In NBUVB group out of 20 patients 9 patients had complete clearance at 16 weeks and 3 had good response 1 patients had poor response. 7 patients discontinued treatment at 12 weeks of therapy due to unknown reasons

Table 17 :Response to treatment in NBUVB group

Results	No. of patients	Percentage	% reduction in PASI score at 16 weeks
Excellent	9	45.00	100
Good	3	15.00	75-100
Moderate	-	-	50-75
Poor response	1	5.00	<50
Discontinued	7	35.00	-

Therefore in NBUVB group 45.00% of patients had excellent response and 15.0 % of patients had good response at 16 weeks. 5.0% had poor response.

RESPONSE TO THERAPY IN TOPICAL GROUP

7 patients had complete clearance at 16 weeks and 13 had good response. None of the patients discontinued therapy.

Therefore in Topical group 15 % of patients had excellent response and 60 % of patients had good response at 16 weeks. 15% had poor response

Table 18: Response to treatment in TOPICAL group

Results	No. of patients	Percentage	% reduction in PASI score at 16 weeks
Excellent	7	35.00	100
Good	13	65.00	75-100
Moderate	-	-	50-75
Poor response	-	-	<50
Discontinued	-	-	-

SIDE EFFECTS

In Methotrexate group

- 3 patients developed nausea
- 1 patient had gastritis

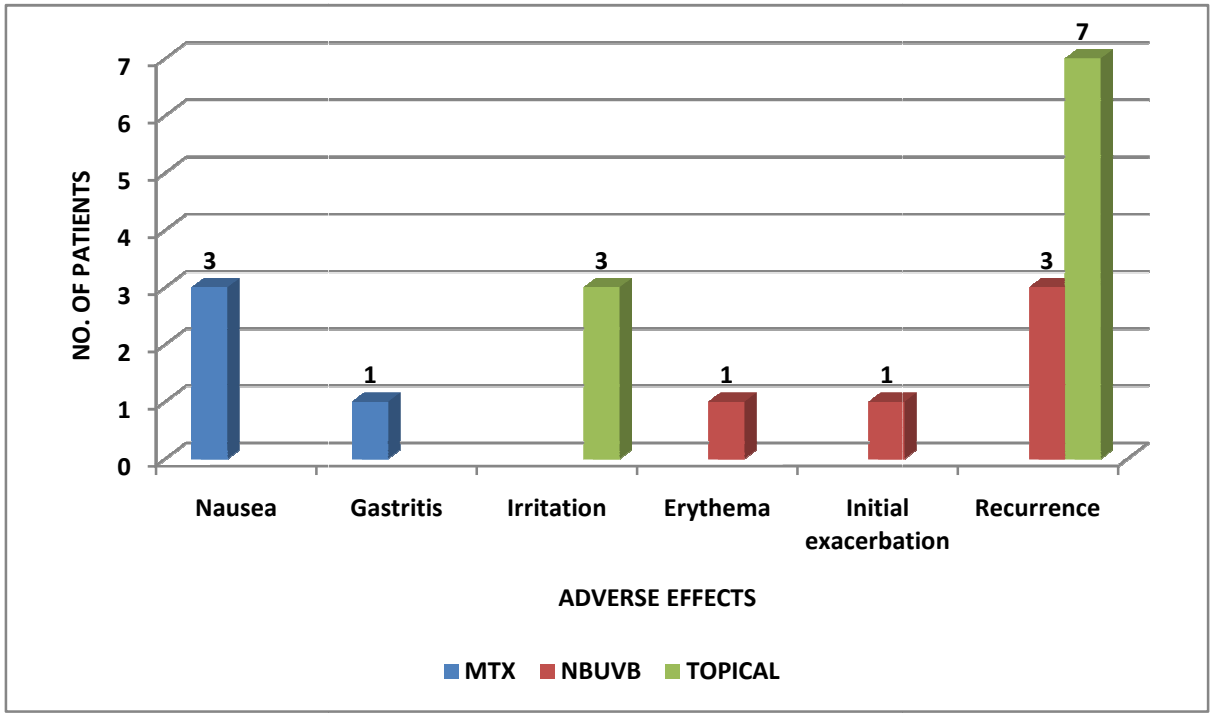
In NBUVB group

- 1 patient developed erythema
- 1 patient had initial exacerbation
- 3 patients had recurrence

In Topical group

- **7** patients had recurrence
- 3 patients developed irritation

Figure 9 :Showing adverse effects in three groups



Dermatology Life Quality Index evaluation in three different groups

A questionnaire assessing the extent to which patients suffer in carrying out day to day activities was used to assess the Dermatology Life Quality Index and the results are tabulated as follows

Table 21 showing Dermatology Life Quality index evaluation

Weeks	Dermatology Life Quality Index points		
	MTX group	NB-UVB group	Topical group
Baseline	35	34	32
4 weeks	23	27	28
8 weeks	17	20	21
12 weeks	11	14	15
16 weeks	4	10	9

Figure 10: Showing improvement in Dermatology Life Quality Index

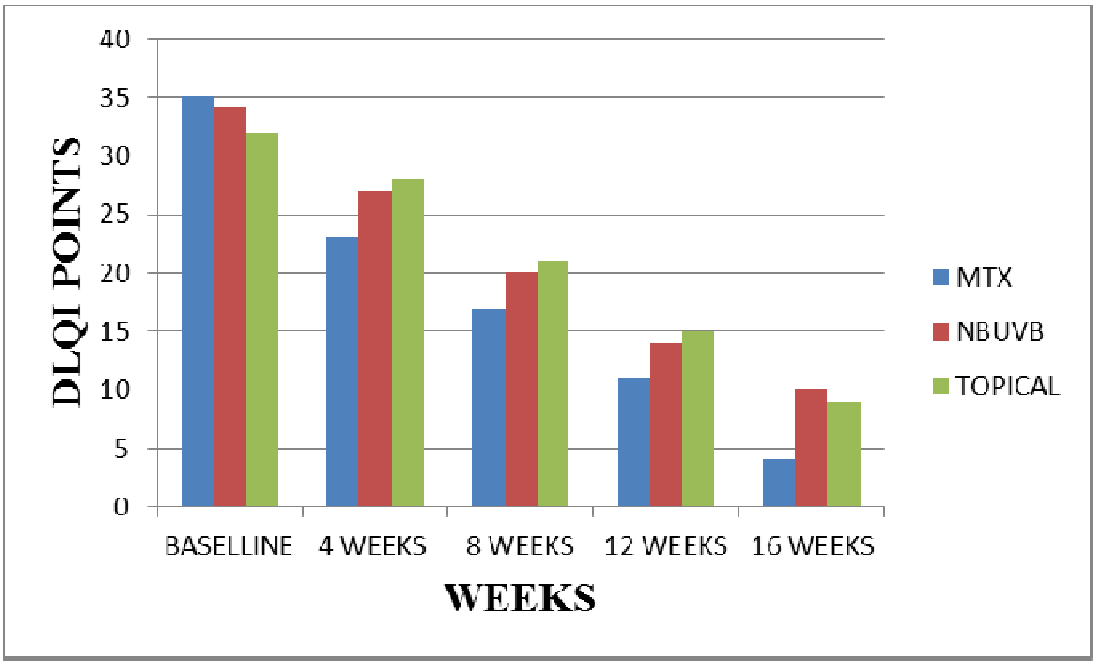


Figure 11: Showing quality of improvement in MTX group

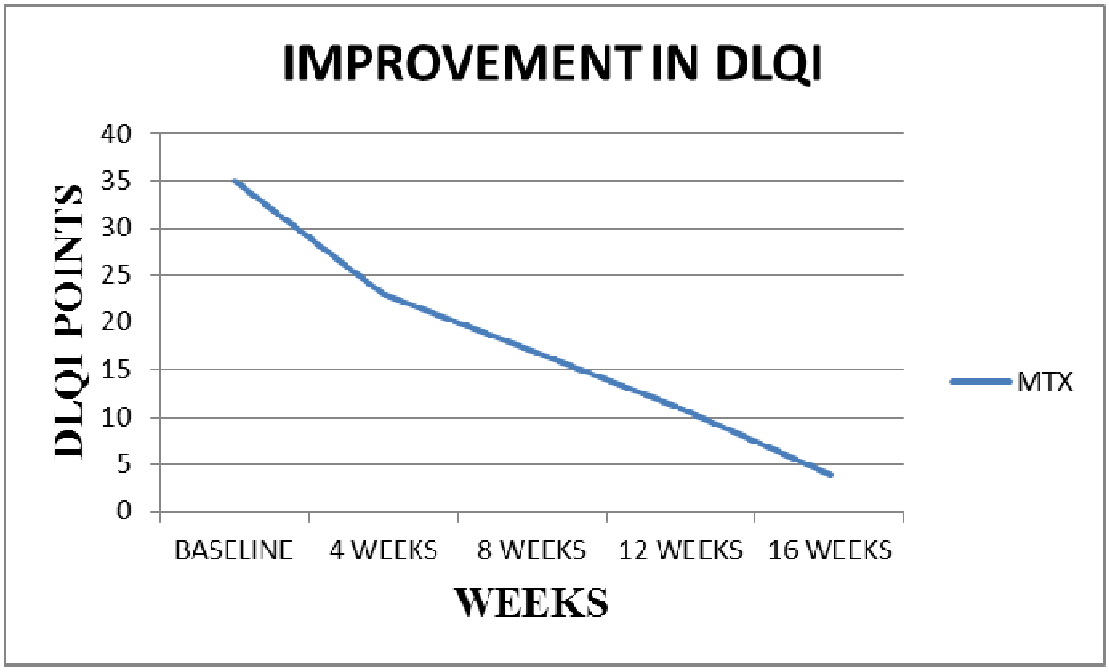


Figure 12: Showing quality of improvement in NBUVB group

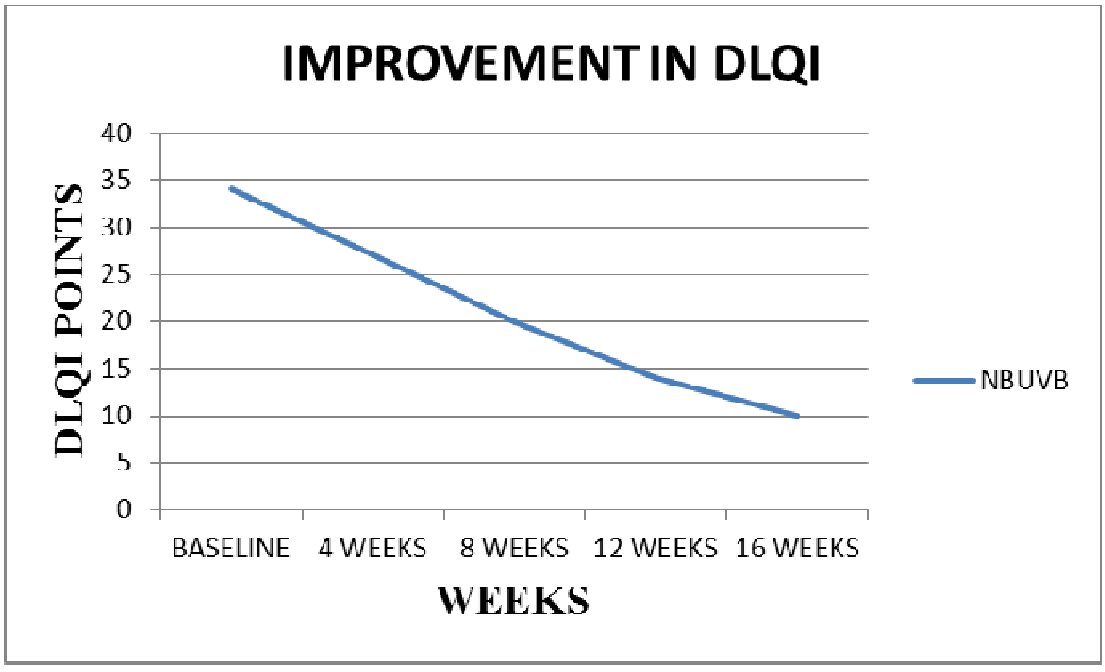
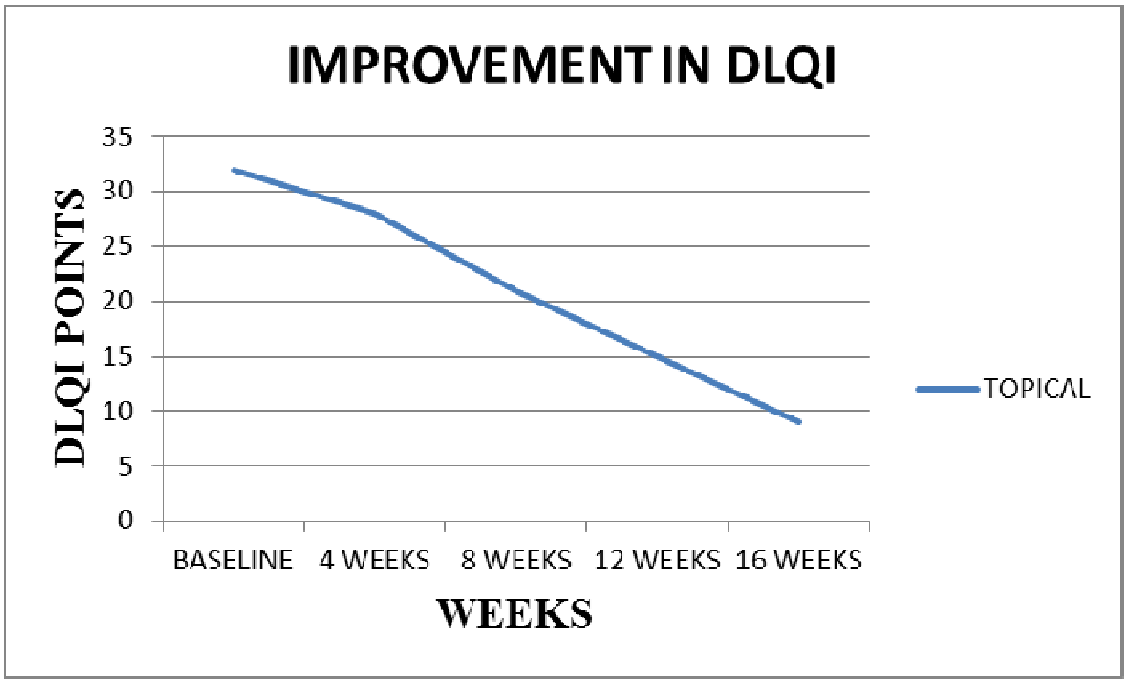
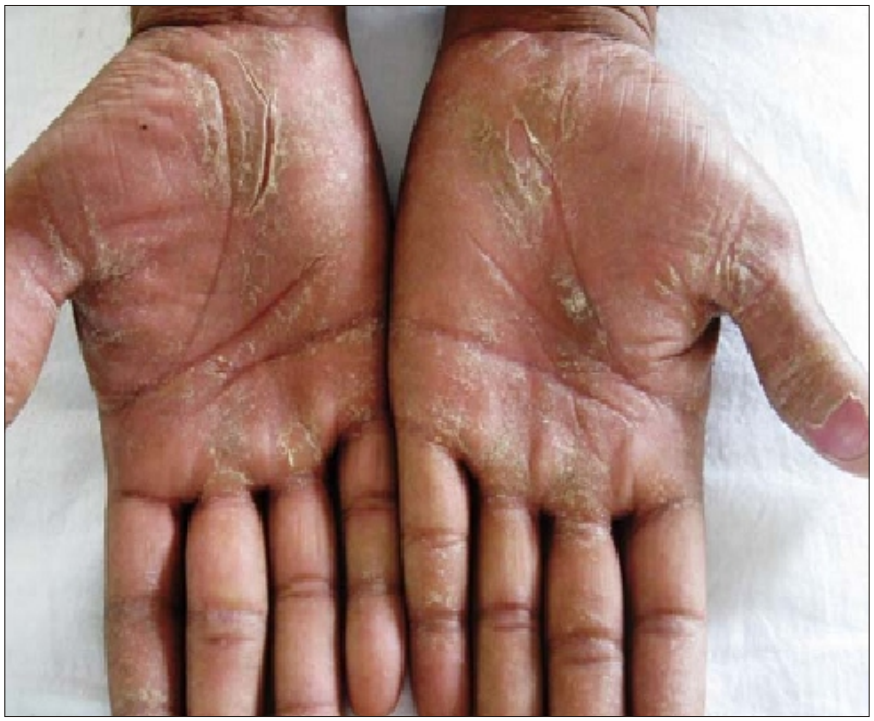
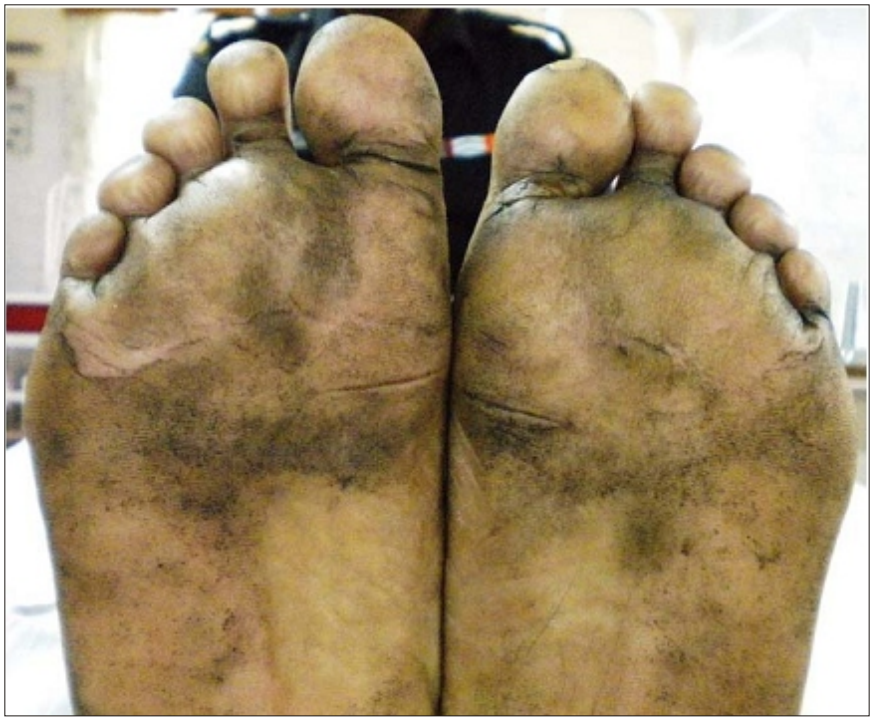


Figure 13: Showing quality of improvement in Topical group

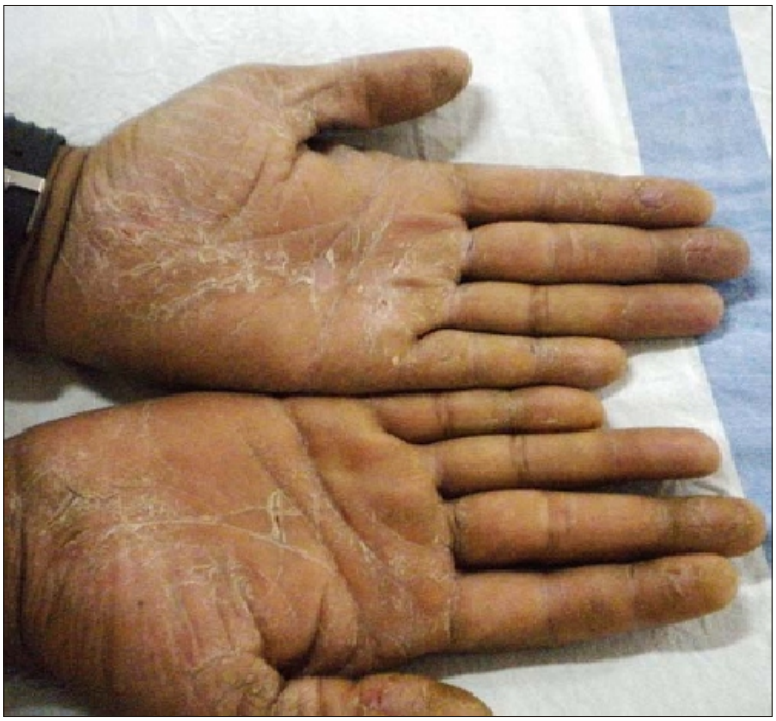


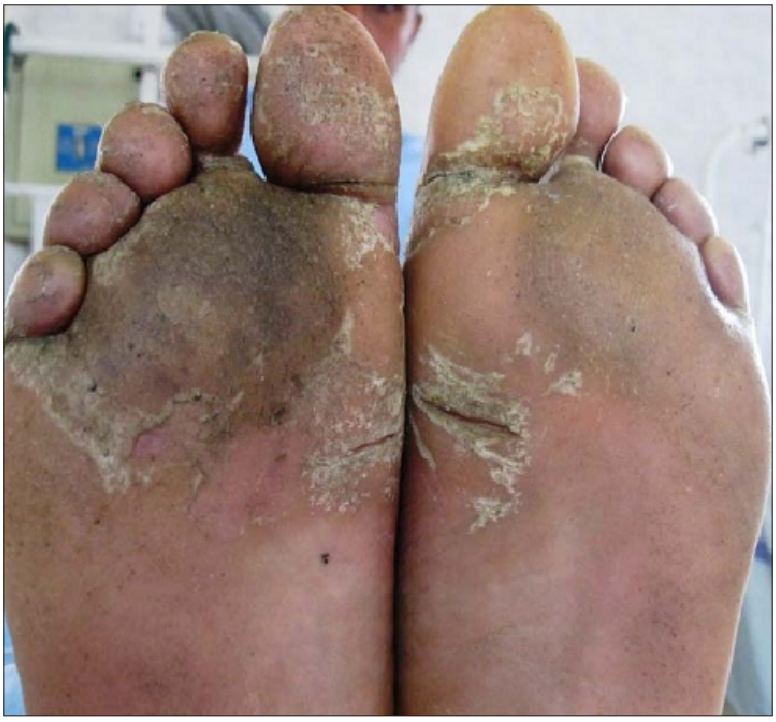
MTX - BASELINE



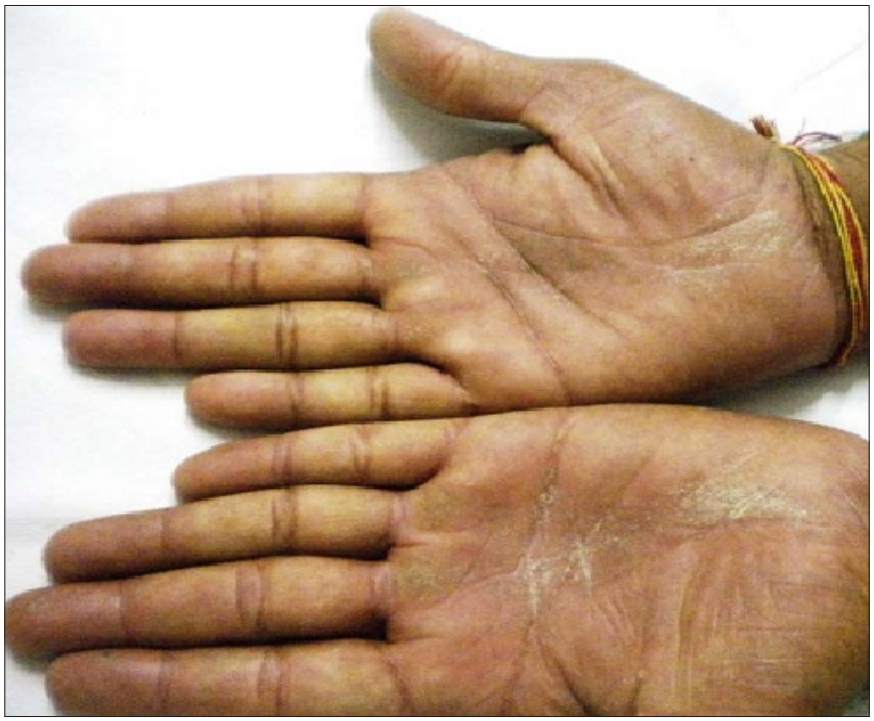


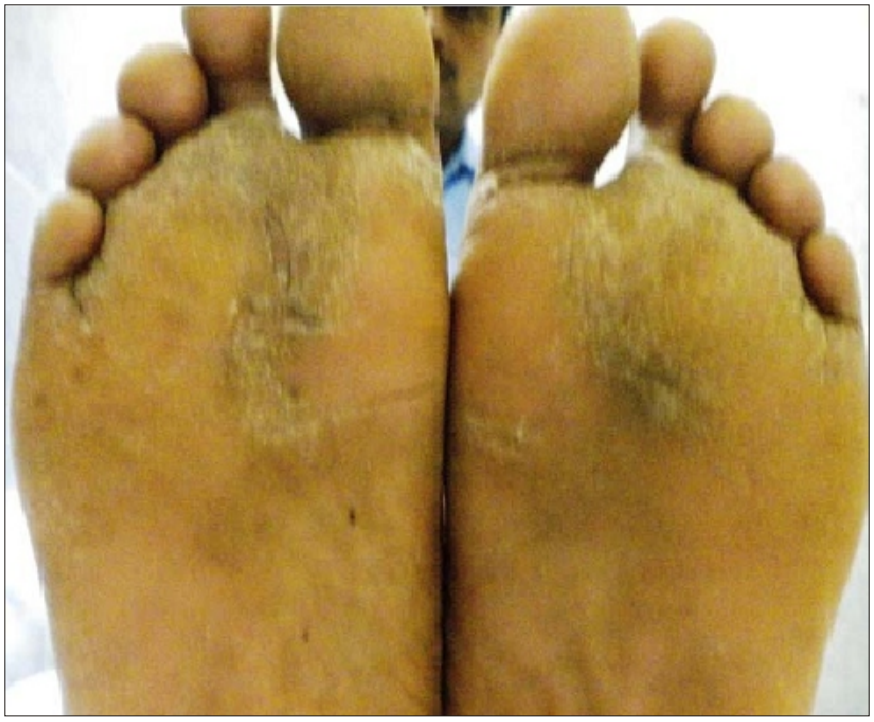
MTX - 4 WEEKS



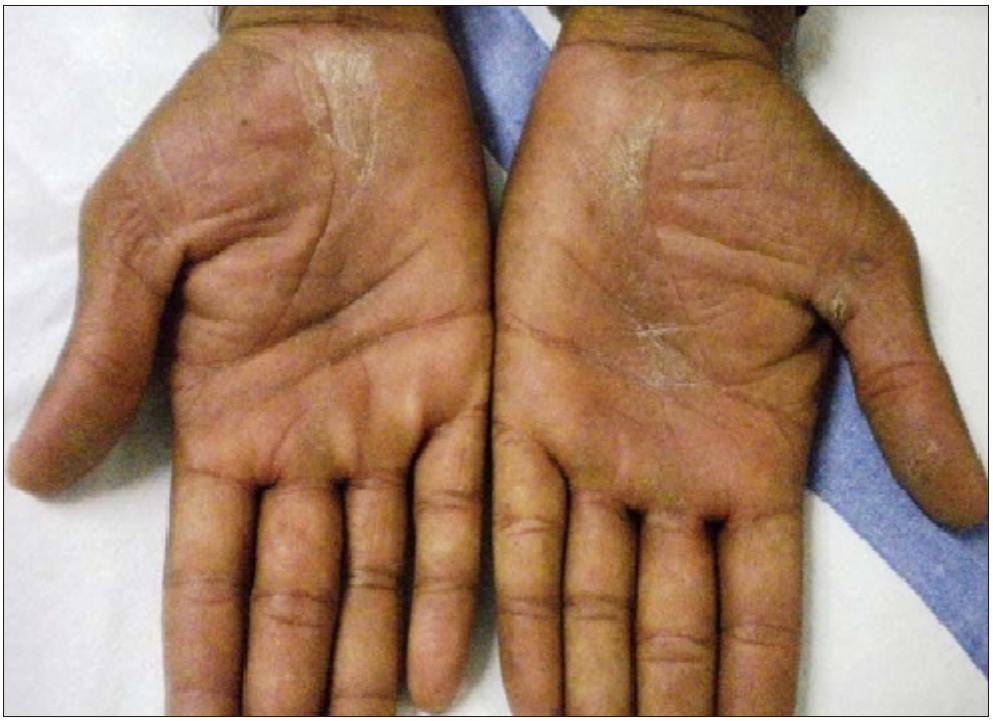


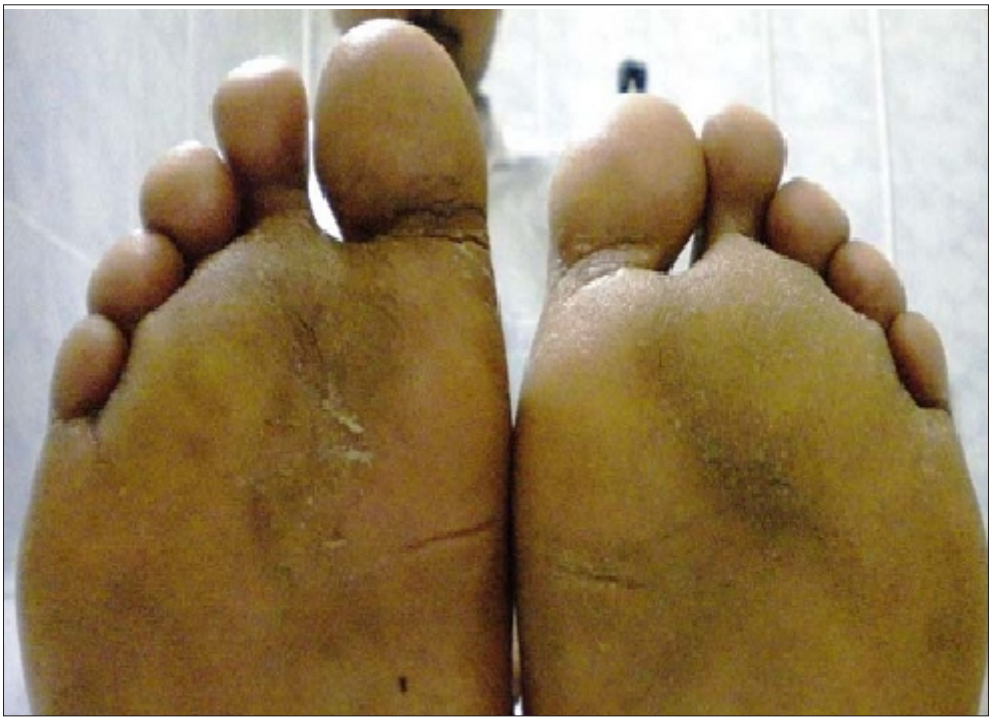
MTX - 8 WEEKS



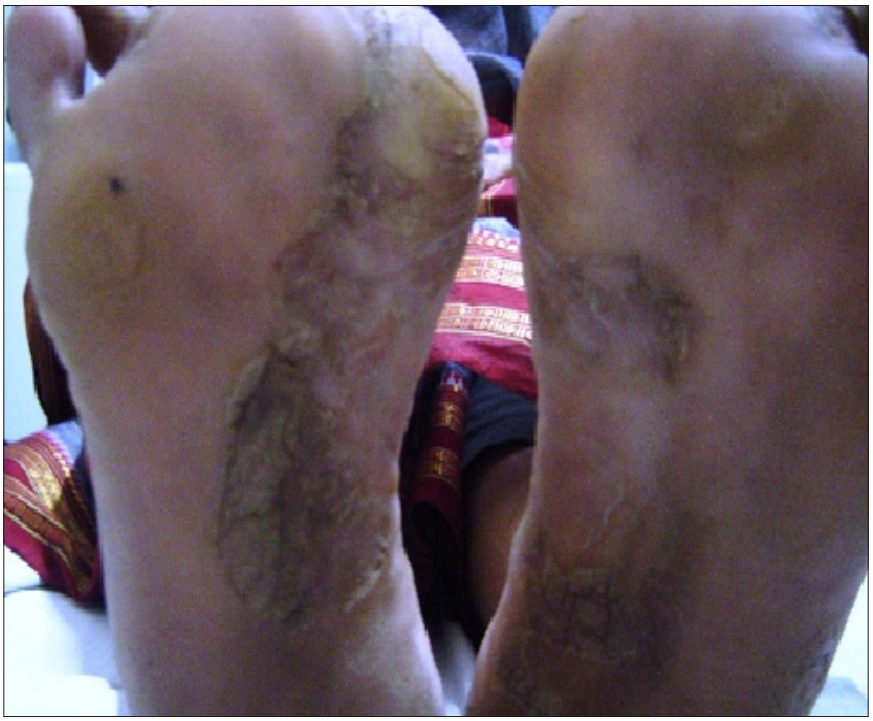


MTX - 16 WEEKS

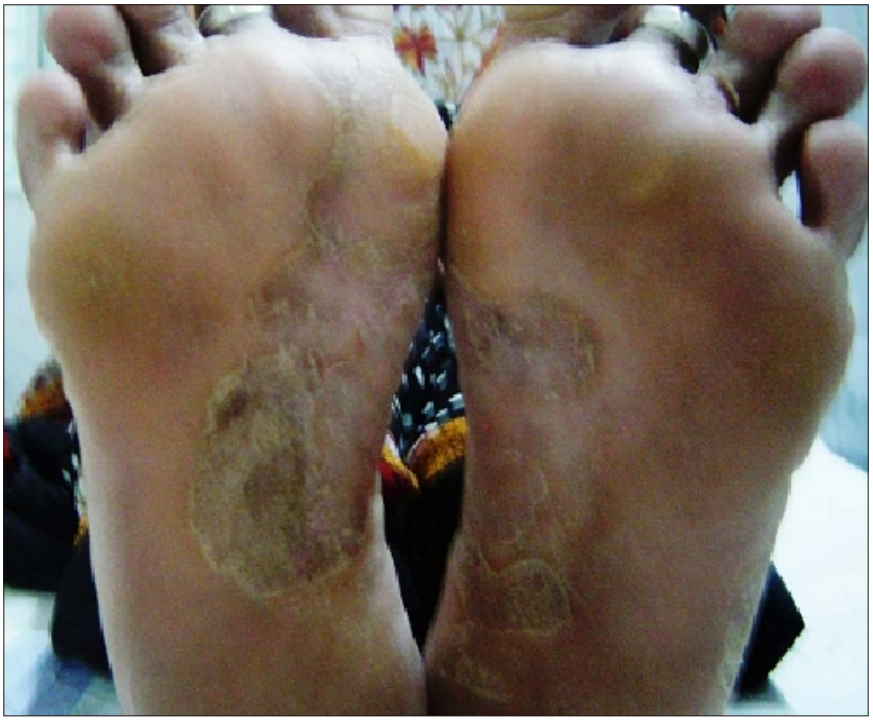




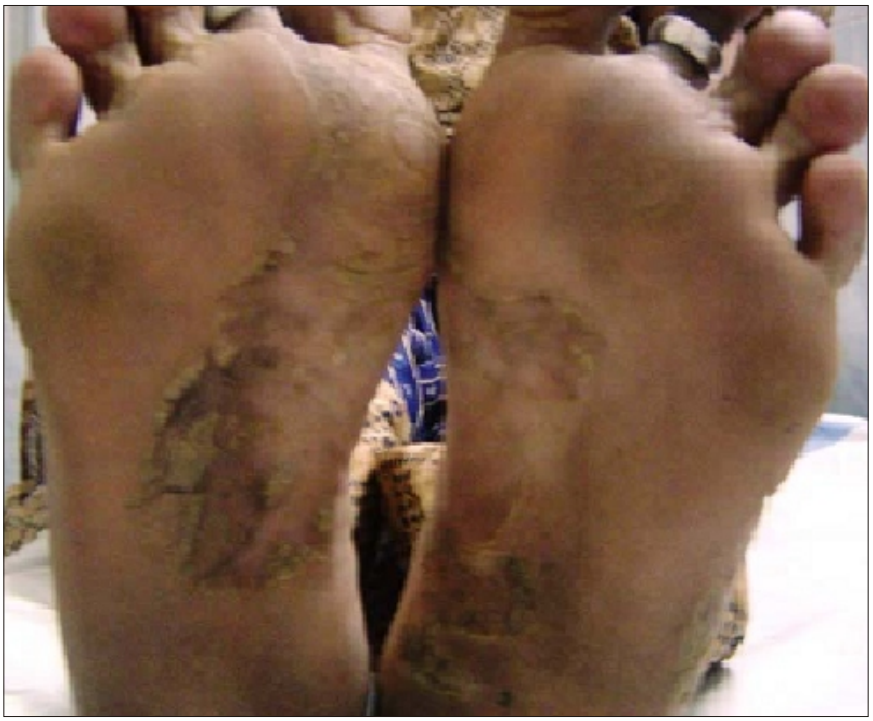
NBUVB - BASELINE



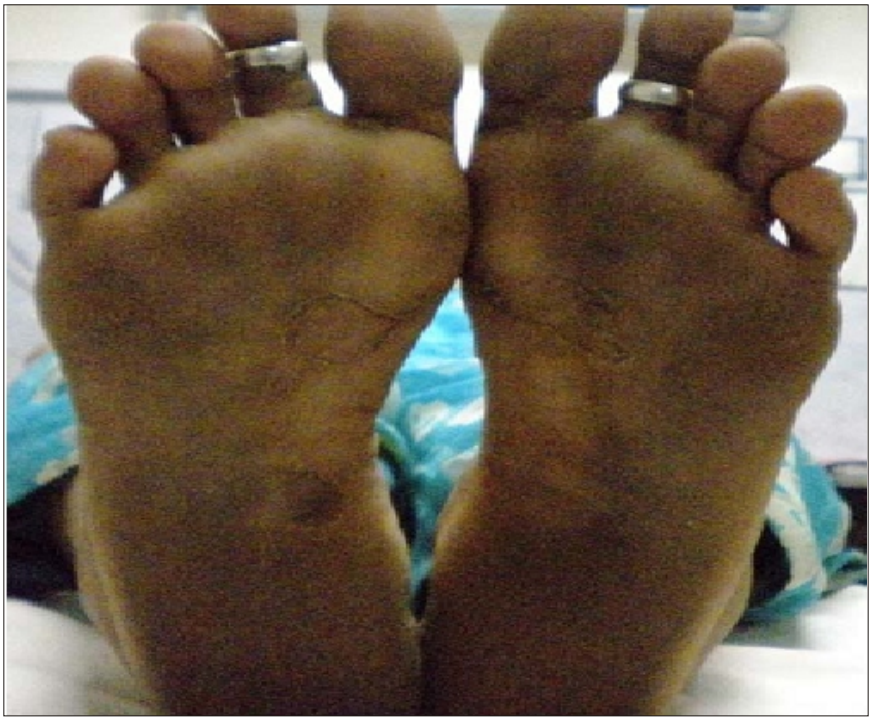
NBUVB - 4 WEEKS



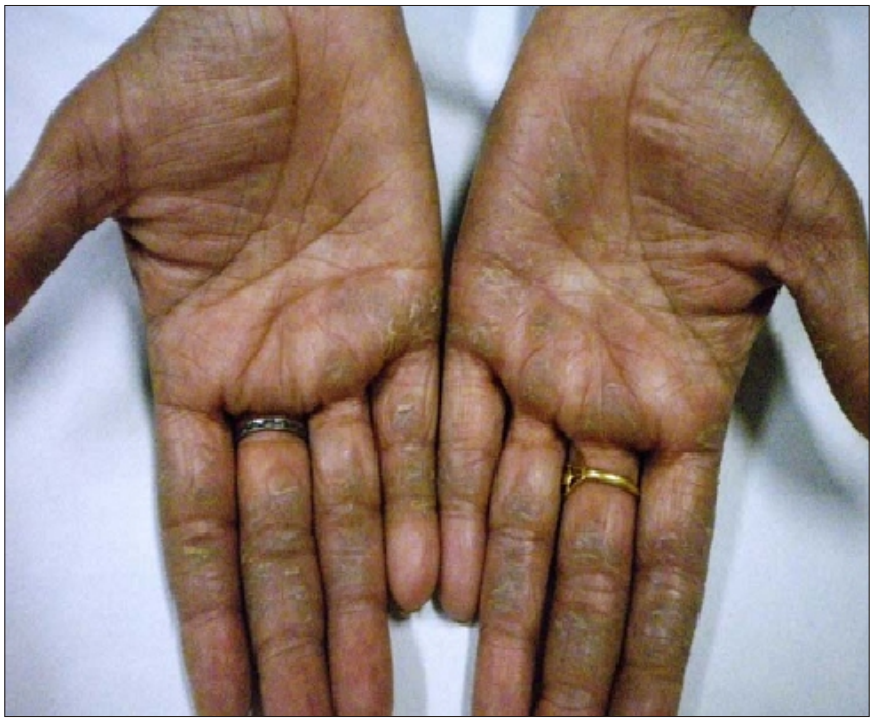
NBUVB - 8 WEEKS



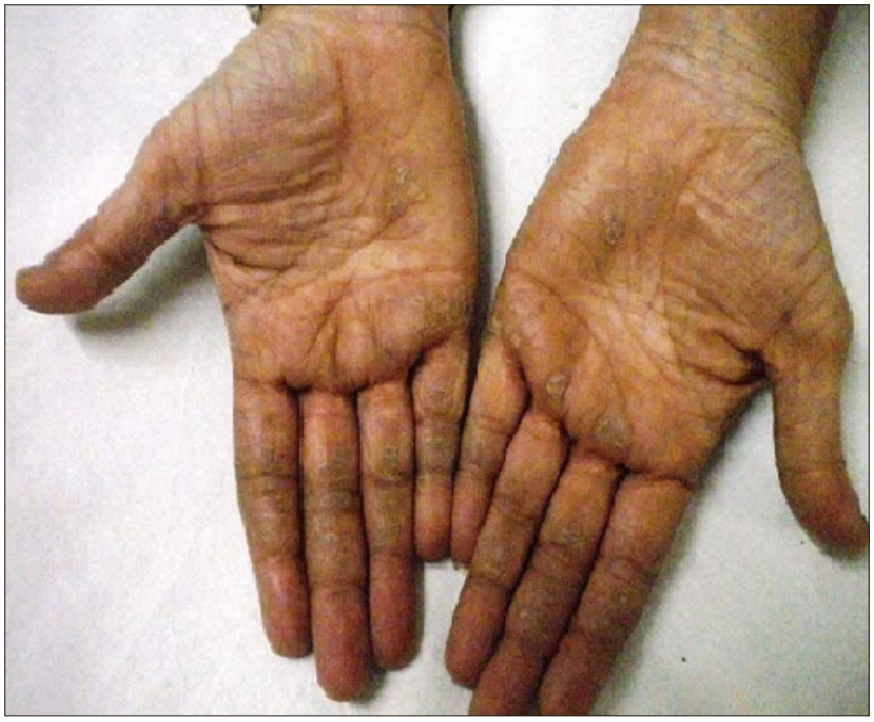
NBUVB - 16 WEEKS



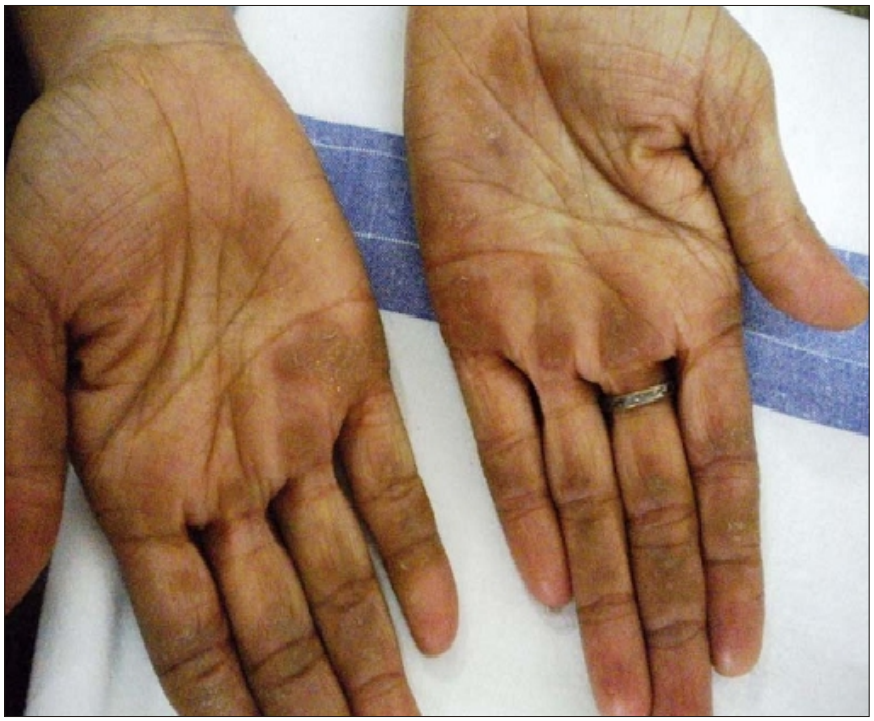
TOPICAL - BASELINE



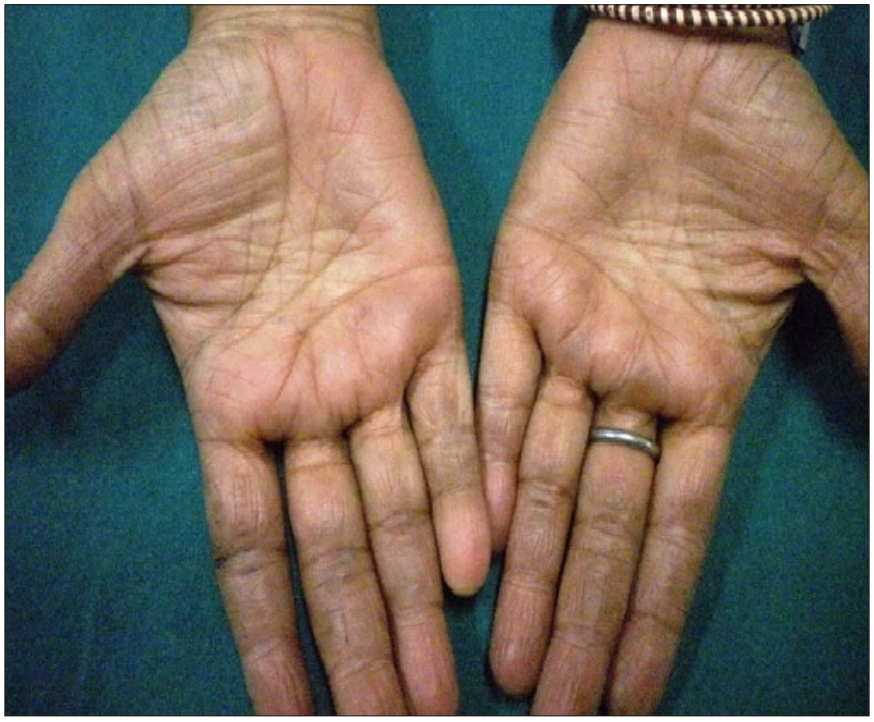
TOPICAL - 4 WEEKS



TOPICAL - 8 WEEKS



TOPICAL - 16 WEEKS



Discussion

DISCUSSION

Palmoplantar psoriasis is a localized form of psoriasis characterized by erythema, hyperkeratosis with surrounding lichenification and coarse scale, resulting in peeling, blistering, crusting, fissuring and bleeding. These symptoms may significantly interfere with activities, inhibiting patients from working with their hands or walking on their feet comfortably leading to major disability and reduction in quality of life. Once established, it might last for decades and can cause impaired dexterity or mobility, as well as discomforting pruritus and pain. This type of psoriasis is also chronic with frequent exacerbation, difficulty in management and resistant to therapy[74,75].

The treatment modalities for psoriasis can be divided into topical, physical and systemic agents. Here in this study we compared the therapeutic response to drugs, one from each of these modalities namely methotrexate, a systemic treatment modality, NB-UVB, a physical treatment modality and a combination of clobetasol propionate with calcitriol ointment as a topical treatment modality. There are very few studies comparing the therapeutic efficacy between these agents and there is no

single study comparing the efficacy of Methotrexate, NB-UVB and Topical Calcitriol 0.0003% with Clobetasol Propionate 0.05% ointment.

We enrolled 60 patients with palmoplantar psoriasis not involving other body areas. They were randomly divided into three groups.

All three groups were well matched in terms of age, duration of lesions and baseline PASI score. They were followed up weekly after initiating treatment. PASI score were calculated at 0, 4, 8, 12 and 16 weeks.

AGE DISTRIBUTION:

Palmoplantar Psoriasis may affect people of all ages. In this study age group ranged from 12 years to 56 years with mean age of 30 years. This was in concurrence with the with the age incidence of earlier studies of Spuls et al[115] which showed mean age of onset 28 years. Similarly, Sharma et al[113] and Lal et al[114] showed highest incidence to be in the second decade.

SEX DISTRIBUTION :

In the current study, male patients constituted the majority. This concurred with most of the Indian studies.[113-115]

The higher incidence in males could be explained by the fact that though there is no strict variation in the occurrence of the disease in both sexes, the male patients come forward for examination and treatment where as, there is a hesitancy on the part of females to come forward for treatment, for fear of social stigma and rejection.[115]

DURATION OF ILLNESS

The duration of illness varied in three groups. In Methotrexate group duration of illness varied from 1 month to 30 months. Similar study by Mehta et al [116] showed where duration of illness between 13-48 months.

In NBUVB group duration of illness varied from 2 months to 30 months. Lal et al[114] showed duration of illness between 18 months to 3 years.

In topical group duration of illness varied from 3 months to 26 months. This correlates with the study by Lafah et al[114]

OCCUPATIONAL STATUS

In this study, the majority of patients were manual labourers. The next majority of patients were housewives, drivers, mechanics and students.

Majority of the patients were manual labourers and housewives which could be attributed to occupational trauma. This is similar to study by Stewart et al [117]and Paul et al [118]

COMPARISON OF METHOTREXATE, NBUVB & TOPICAL CALCITRIOL WITH CLOBETASOL PROPIONATE BASED ON PASI SCORING

In methotrexate group the mean baseline PASI score is 30.98 and mean PASI score at 16 weeks is 0.49. Therefore there is 98.4% reduction in PASI score at end of 16 weeks. Dhir et al[112] showed PASI reduction of 93% in 12 weeks.

In NBUVB group the mean baseline PASI score is 28.19 and at mean PASI score at 16 weeks is 1.76. PASI reduction was 93.75% at the end of 16 weeks. Dayal et al [120] showed 84% PASI reduction in a 12 week study.

In Topical group the mean baseline PASI score is 28.66 and mean PASI score at 16 weeks is 1.45. Therefore there is 94.94% reduction in PASI score at end of 16 weeks. Lafah et al[123] showed PASI reduction of 86% in 16 weeks.

PASI 75 was attained at 8-12 weeks in Methotrexate group and PASI 75 was attained at 12-16 weeks in NBUVB group. This is in concurrence with Dhir et al[112]. PASI 75 was attained in 10-12 weeks in Topical group in close concordance with the study by Lafah et al[123.]

All three groups showed appreciable clearance in lesions at the end of 16 weeks but it took a longer time to achieve PASI 75 in NBUVB group and topical group than in Methotrexate group in concurrence with Paul et al[120] and Lafah et al[123].

SIDE EFFECTS

Nausea and gastritis were observed as side effects in Methotrexate group as in Dhir et al[112]. Other side effects which were reported in that study were not present here.

In NBUVB group, the side effects noted were erythema followed by pruritus. This was seen to be similar to studies by Paul et al[119] and Asawanonda et al[122]. Initial exacerbation was noted in 1 of our patients in NBUVB group, but newer lesions ceased to appear with continuation of

therapy. This correlated with Piskin et al, Woo WK et al and Collins et al[125-127].

In Topical group, irritation was noted as a side effect. This was in concordance with Gallini et al [124]

RELAPSE OF DISEASE

No relapse cases were reported in methotrexate group in the follow-up period of 8 weeks. Dhir et al[112] reported 2 relapse cases in a follow-up period of 1 year.

NBUVB group had 3 relapse cases. Dayal et al[120] reported 2 relapse cases among 46 patients treated with NB-UVB and followed up for 1 year.

Topical group had 7 relapse cases. Lafah et al[123] reported 3 relapse cases among 60 patients.

COMPLIANCE

Compliance and adherence to treatment regime was better in methotrexate group as no drop-outs were reported. This was concurrent with studies by Dhir et al[112] and Lafah et al[123]. In NB-UVB group follow-up was lost with seven patients. This correlated with the study by Dayal et al[120]

Conclusion

CONCLUSION

- Methotrexate therapy is the most effective modality of treatment in palmoplantar psoriasis.

- NBUVB therapy has equal efficacy to topical clobetasol with calcitriol therapy in our study.

- The mean PASI reduction is almost equal for both NBUVB therapy and topical clobetasol with calcitriol therapy.

- DLQI questionnaire proved to be a useful tool in assessing patient's subjective improvement after initiation of treatment

- There were no dropouts in methotrexate and topical therapy group compared to NB-UVB group.

- When NBUVB and Topical Clobetasol and Calcitriol are compared there is no statistically significant difference in mean PASI score reduction at 16 weeks.

- Based on compliance and adherence to treatment, topical clobetasol with calcitriol therapy scores over the NBUVB therapy.

- When methotrexate therapy is compared with NB-UVB and topical clobetasol with calcitriol ointment therapy, the rate of clearance of lesions in latter groups were poor.

- All the side effects noted in this study were minor and they were treated conservatively.

- This shows that all three treatment groups namely systemic methotrexate, NB-UVB phototherapy and topical clobetasol with calcitriol ointment achieved >75% or complete clearance at end of 16 weeks. In methotrexate group clearance of lesions was faster with less side effects.

- In NBUVB and topical clobetasol with calcitriol treatment groups lesions took longer time to resolve and also recurrence of lesions were reported.

- Compliance was less with NB-UVB group among the three groups.

- Post treatment follow-up visits were better among the methotrexate group and topical clobetasol with calcitriol ointment group.

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Annexures

PATIENT CONSENT FORM

Title of the study : PALMOPLANTAR PSORIASIS – A COMPARATIVE THERAPEUTIC STUDY

Name of the Participant :

Name of the Principal Investigator : Dr. R. SATHYA NARAYANAN

Name of the Institution : Department of Dermatology,

Rajiv Gandhi Government General Hospital,

Chennai

Patient Enrollment no :

Documentation of the Informed Consent : (legal representative can sign if the participant is minor or incompetent)

I _____ have read/it has been read for me, the information in this form. I was free to ask any questions and they have been answered. I am over 18 years of age and exercising my free power of choice, hereby give my consent to be included as a participant in the study.

1. I have read and understood this consent form and the information provided to me.
2. I have had the consent document explained in detail to me.
3. I have been explained about the nature of my study.
4. My rights and responsibilities have been explained to me by the investigator.
5. I agree to cooperate with the investigator and I will inform her immediately if I suffer from unusual symptoms.
6. I have not participated in any research study at any time.
7. I am aware of the fact that I can opt out of the study at any time without having to give any reason and this will not affect my future treatment in this hospital.
8. I hereby give permission to the investigators to release the information obtained from me as a result of participation in this study to the regulatory authorities, government agencies, and Institutional Ethics Committee. I understand that they are publicly presented.
9. My identity will be kept confidential if my data are publicly presented.
10. I am aware that if I have any question during this study, I should contact the concerned investigator

Participant's Initials : _____

Name and signature/thumb impression of the participant (or legal representative if participant is minor or incompetent)

_____ _____ _____

Name Signature Date

Name and signature of impartial witness (required for illiterate patients)

_____ _____ _____

Name Signature Date

Address and contact number of the impartial witness :

Name and signature of the investigator or his representative obtaining consent:

_____ _____ _____

Name Signature Date

ஆராய்ச்சி ஒப்புதல் கடிதம்

ஆராய்ச்சிதலைப்பு:

பெயர் :தேதி :

வயது :உள்நோயாளிஎண் :

பால் :ஆராய்ச்சிசேர்க்கைஎண் :

**மருத்துவர்மேற்கொள்ளபோகும்பரிசோதனைகளையும்,
சிகிச்சைமுறைகளையும்,
அதன்பலன்மற்றும்பக்கவிளைவுகளையும்மிகதெளிவாக,
எளியமுறையில்விளக்கிக்கூறினார்.எனக்குவிருப்பமில்லாதபட்சத்தில்
ஆராய்ச்சியிலிருந்துஎந்நேரமும்விலகலாம்என்பதையும்மருத்துவர்
மூலம்அறிந்துக்கொண்டேன்.மருத்துவர்மேற்கொள்ளும்ஆராய்ச்சியில்
பங்கேற்கயாருடையகட்டாயமுமின்றிமுழுமனதுடனும்,
சுயநினைவுடனும்சம்மதிக்கிறேன்.இந்தஆராய்ச்சிஒப்புதல்கடிதத்தில்
உள்ளவிவரங்களைநன்குபுரிந்துகொண்டேன்.எனதுஉரிமைகள்மற்றும்
கடமைகள்ஆராய்ச்சியாளர்மூலம்விளக்கப்பட்டது.
நான்ஆராய்ச்சியாளருடன்ஒத்துழைக்கசம்மதிக்கிறேன்.எனக்கு
ஏதேனும்உடல்நலக்குறைவு ஏற்பட்டால் ஆராய்ச்சியாளரிடம்
தெரிவிப்பேன்.நான்வேறுஎந்தஆராய்ச்சிலும்தற்சமயம்இடம்
பெறவில்லைஎன்பதை தெரிவித்துக்கொள்கிறேன்.
இந்தஆராய்ச்சியின்தகவல்களைவெளியிடசம்மதிக்கிறேன்.அப்படி
வெளியிடும்போதுஎன்அடையாளம்வெளிவராதுஎன்பதைஅறிவேன்.
எனக்குஇந்த ஒப்புதல்கடிதத்தின்நகல்கொடுக்கப்பட்டது.**

கையொப்பம்

PROFORMA

Name: **Date:**

Age: **OP No:**

Sex: **Case No:**

Occupation:

Address:

HISTORY:

Complaints:

Duration:

Itching: Yes/No

H/o Previous treatment: Topical/Systemic

PAST HISTORY:

Diabetes Mellitus	Hypertension	Tuberculosis
Photosensitivity	Cutaneous Malignancy	Radiotherapy

DRUG TAKEN FOR ANY OTHER CONDITION:

If yes	Name of the drug	Duration of treatment

FAMILY HISTORY:

PERSONAL HISTORY:

Smoking:

Alcohol:

MENSTRUAL HISTORY:

PREGNANCY:

LACTATION:

GENERAL EXAMINATION:

Pallor

Icterus

Edema

Pulse

Blood Pressure

Weight

SYSTEMIC EXAMINATION:

CVS

RS

P/A

CNS

ENT

DENTAL

DERMATOLOGICAL EXAMINATION:

Skin lesions	Site
	Morphology
	Other sites
	Mucous membranes
	Scalp
	Hair
	Nails

AREA & SEVERITY ASSESSMENT BY PASI SCORING:

Erythema/ Infiltration/ Desquamation Scoring	**Area scoring**
0- Nil	0- Nil
1- Mild	1- 0-9%
2- Moderate	2- 10-29%
3- Severe	3- 30-49%
4- Very severe	4- 50-69%
	5- 70-89%
	6- 90-100%

PASI will be calculated as follows

$PASI = 0.2(E_U+I_U+D_U)AU + 0.4(E_L+I_L+D_L)AL$

A – Area U- Upper limb L- Lower limb

INVESTIGATIONS:

Total count:

Differential count:

ESR:

Hb:

Blood sugar

Urea

Creatinine:

Serum calcium:

VDRL:

VCTC:

LFT:

PASI SCORING

Week	PASI score	% Improvement
0 4 8 12 16		

MASTER CHART – METHOTREXATE

S. NO	AGE	SEX	DURATION	OCCUPATION	SITE	NAIL	JOINT	BODY	SCALP	PASI 0	PASI 4	PASI 8	PASI 12	PASI 16	SIDE EFFECTS	RECURRENCE
1	33	F	2Y	HOUSEWIFE	PALMS & SOLES	P	N	N	N	34	22.2	10.8	4.6	0	N	N
2	36	F	8M	HOUSEWIFE	SOLES	P	N	N	N	20.2	12	5.4	1.2	0	N	N
3	43	M	7M	LABOURER	SOLES	N	N	N	N	20	10.2	4.4	0	0	N	N
4	56	M	2Y 6M	FARMER	PALMS & SOLES	O, SUH	N	N	N	32.4	17.6	8.8	7.6	DISC0NTINUED	GASTRITIS	N
5	31	M	1Y	LABOURER	PALMS & SOLES	N	N	N	N	33.6	18.8	9.8	3.6	0	N	N
6	38	M	1Y 3M	MECHANIC	SOLES	O,R	N	N	N	29.4	15.4	7.8	2.2	0	N	N
7	50	M	8M	HOUSEWIFE	PALMS & SOLES	SUH	N	N	N	31.4	16.2	8.6	5.4	0	NAUSEA	N
8	48	F	1Y 7M	MECHANIC	PALMS & SOLES	N	N	N	N	37.4	19.2	10.2	3.8	0	N	N
9	37	M	1Y 1M	LABOURER	PALMS & SOLES	N	N	N	N	30.2	15	7.2	5.2	2.6	N	N
10	25	M	3M	PROFESSIONAL	PALMS & SOLES	N	N	N	N	31.2	16	9.2	4.4	0	N	N
11	48	M	9M	DAILY WAGER	SOLES	N	N	N	N	29.6	14.8	7.2	3.6	0	N	N
12	37	F	6M	TEACHER	PALMS & SOLES	N	N	N	N	33.8	17	8.8	6.2	3.2	NAUSEA	N
13	28	M	2M	HOUSEWIFE	PALMS & SOLES	O,SUH	N	N	N	34.6	17.2	8.8	5.4	1.4	N	N
14	40	F	3M	MECHANIC	PALMS & SOLES	N	N	N	N	37.8	19	10.2	5.4	0	N	N
15	33	M	4M	LABOURER	PALMS	N	N	N	N	27	14	6.8	0	0	N	N
16	46	M	1Y, 2M	HOUSEWIFE	PALMS	P	N	Y	N	29	14	6.2	0	0	N	N
17	35	F	10M	HOUSEWIFE	PALMS & SOLES	N	N	N	N	29.8	15.2	7.8	2.4	0	N	N
18	29	F	1Y 9 M	PROFESSIONAL	PALMS & SOLES	N	N	N	N	36.2	18.6	10.2	3.4	0	N	N
19	22	M	1Y 4M	STUDENT	PALMS & SOLES	N	N	N	N	39.4	20	13.4	6.8	2.2	NAUSEA	N
20	39	F	1M	HOUSEWIFE	PALMS & SOLES	P	N	N	N	27.6	14.4	7.6	3	0	N	N

MASTER CHART – NBUVB

S.NO	AGE	SEX	DURATION	OCCUPATION	SITE	NAIL	JOINT	BODY	SCALP	PASI 0	PASI 4	PASI 8	PASI 12	PASI 16	SIDE EFFECTS	RECURRENCE
1	39	F	1Y, 2M	HOUSEWIFE	PALMS & SOLES	N	N	N	N	29.4	19.6	12.4	5.6	2.6	INITIAL EXACERBATION	Y
2	36	M	6M	MECHANIC	SOLES	N	N	N	N	27.6	18.4	12.6	DISCONTINUED		N	LOST FOLLOWUP
3	22	M	3M	STUDENT	PALMS	N	N	N	N	22.4	12.4	6.4	0	0	N	N
4	50	F	1Y, 6M	HOUSEWIFE	PALMS & SOLES	N	N	N	N	33.8	22.4	18.4	DISCONTINUED			LOST FOLLOWUP
5	36	F	1Y	HOUSEWIFE	PALMS & SOLES	N	N	N	N	31.2	18.8	9.4	4.6	0	N	N
6	32	F	8M	TYPIST	PALMS	N	N	N	N	25.6	15.4	7.8	3.6	0	N	N
7	47	F	1Y, 5M	HOUSEWIFE	SOLES	N	N	N	N	30.4	22.8	17.2	DISCONTINUED		N	LOST FOLLOWUP
8	30	F	1Y, 8M	CLERICAL	PALMS & SOLES	N	N	N	N	36	19.6	9.8	4.6	0	N	N
9	49	M	1Y	DAILY WAGER	SOLES	N	N	N	N	29.2	17.6	12.8	DISCONTINUED		N	LOST FOLLOWUP
10	53	M	2Y, 4M	DAILY WAGER	PALMS & SOLES	SUH	N	N	N	30.4	20.8	14.4	DISCONTINUED		ERYTHEMA	LOST FOLLOWUP
11	56	M	2Y,6M	WATCHMAN	PALMS	N	N	N	N	22.8	16.8	9.8	DISCONTINUED		N	LOST FOLLOWUP
12	33	F	1Y	HOUSEWIFE	PALMS	N	N	N	N	23.8	12	6.4	2.8	0	N	N
13	29	F	1Y, 8M	TYPIST	SOLES	P	N	N	N	24.8	15.4	8.8	4	0	N	N
14	39	F	7M	HOUSEWIFE	PALMS & SOLES	O	N	N	N	36.8	19	10.4	7.2	3.4	N	Y
15	22	F	2M	STUDENT	SOLES	N	N	N	N	29.4	15	8.8	5.4	2.2	N	N
16	20	F	2M	STUDENT	PALMS & SOLES	P	N	Y	N	23.8	13	6.8	2.4	0	N	N
17	50	M	8M	BUSINESS	PALMS	SUH, P	N	N	N	26.8	18.4	13.6	DISCONTINUED		N	LOST FOLLOWUP
18	38	M	1Y, 5M	MECHANIC	PALMS & SOLES	R	N	N	N	26.4	16.4	11.6	6.4	3	N	Y
19	30	F	7M	HOUSEWIFE	PALMS & SOLES	N	N	N	N	27.4	18	11.2	7	2.8	N	N
20	26	F	5M	IT	PALMS & SOLES	N	N	N	N	22.8	12	7.6	2.8	0	N	N

MASTER CHART – TOPICAL CLOBETASOL + CALCITRIOL

S.NO	AGE	SEX	DURATION	OCCUPATION	SITE	NAIL	JOINT	BODY	SCALP	PASI 0	PASI 4	PASI 8	PASI 12	PASI 16	SIDE EFFECTS	RECURRENCE
1	38	F	2Y	HOUSEWIFE	PALMS & SOLES	P	N	N	N	32	20.2	10.8	5.6	2.4	N	Y
2	43	M	5M	LABOURER	SOLES	O	N	N	N	26.4	13	6.8	2.2	0	N	N
3	41	M	9M	LABOURER	PALMS & SOLES	N	N	N	N	31.2	16.2	9.8	4.4	2.2	N	N
4	48	M	1Y 6M	FARMER	PALMS & SOLES	O,SUH	N	N	N	30.4	14.8	9	5.2	3	N	N
5	37	F	8M	HOUSEMAID	SOLES	N	N	N	N	24.8	11.6	7.8	3.6	0	IRRITATION	N
6	35	M	1Y, 7M	MECHANIC	SOLES	O,R	N	N	N	22.8	14.4	7.8	5.4	2.6	N	Y
7	29	M	3M	HOUSEWIFE	PALMS	SUH	N	N	N	21.4	10.4	5.6	2.8	0	N	N
8	44	F	9M	MECHANIC	SOLES	N	N	N	N	22.8	16.4	11.2	6.4	3.2	N	Y
9	46	M	2Y, 2M	LABOURER	PALMS & SOLES	N	N	N	N	28.4	16.4	10	6.4	3	N	Y
10	25	F	4M	TEACHER	PALMS & SOLES	N	N	N	N	19.2	12	6	2.8	0	N	N
11	39	M	9M	DAILYWAGER	PALMS & SOLES	O	N	N	N	26.8	14.8	8	4.4	1.2	IRRITATION	N
12	37	M	1Y, 2M	LABOURER	PALMS & SOLES	N	N	N	N	32.8	16.4	9.2	6	3	N	Y
13	30	M	5M	MECHANIC	PALMS & SOLES	N	N	N	N	27.2	15.6	8.8	5	1.8	N	Y
14	23	M	3M	STUDENT	PALMS & SOLES	N	N	N	N	30.4	16.8	10.2	5.4	0	N	N
15	35	M	10M	LABOURER	PALMS & SOLES	N	N	N	N	27	13	6.8	3.4	0.8	N	N
16	43	F	1Y, 7M	HOUSEWIFE	PALMS & SOLES	R	N	Y	N	29.4	15	7.8	5	1.4	IRRITATION	N
17	29	F	11M	HOUSEWIFE	PALMS & SOLES	R	N	N	N	30.6	15.2	7.8	2.4	0	N	N
18	36	M	1Y, 9M	MECHANIC	PALMS & SOLES	N	N	N	N	25.6	16.2	10.2	7.8	4.2	N	N
19	12	M	4M	STUDENT	SOLES	N	N	N	N	22.4	15	13.4	6.8	2.2	N	N
20	31	M	11M	LABOURER	SOLES	SUH	N	N	N	21.6	14.8	8.8	5.2	0	N	Y

ABBREVIATIONS

PPP	–	Palmoplantar Psoriasis
Mtx	–	Methotrexate
NBUVB	–	Narrow band ultraviolet B
UV-A	–	Ultraviolet A
UV-B	–	Ultraviolet B
HLA	–	Human Leucocyte Antigen
NSAID's	–	Non Steroidal Anti-inflammatory Drugs
IL	–	Interleukin
TNF	–	Tumor Necrosis Factor
NOS	–	Nitric Oxide Synthase
PUVA	–	Psoralen Ultraviolet A
GRα	–	Glucocorticoid Receptor α
GRE	–	Glucocorticoid Response Elements
RXR	–	Retinoid X Receptor
MED	–	Minimum Erythema Dose
PAN	–	PolyarteritisNodosa
PIIINP	–	Procollagen III aminopeptide
DLQI	–	Dermatology Life Quality Index

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI -3

EC Reg. No. ECR/270/Inst./TN/2013
Telephone No. : 044 25305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr.R. Sathya Narayanan,
PG in M.D. Dermatology, Venerology, Leprology
Department of Dermatology,
Madras Medical College, Chennai -3.

Dear Dr.R. Sathya Narayanan,

The Institutional Ethics Committee of Madras Medical College reviewed and discussed your application for approval of the proposal entitled **"PALMOPLANTAR PSORIASIS – A COMPARATIVE THERAPEUTIC STUDY"** No. 09112013

The following members of Ethics Committee were present in the meeting held on 13.11.2013 conducted at Madras Medical College, Chennai -3.

1. Dr. G. Sivakumar, MS FICS FAIS -- Chairperson
2. Prof. R. Nandini, MD -- Member Secretary
   Director, Instt.of Pharmacology, MMC, Ch-3
3. Prof. Ramadevi, MD -- Member
   Director i/c, Instt.of Biochemistry, MMC, Chennai.
4. Prof. P. Karkuzhali, MD -- Member
   Professor, Instt.of Pathology, MMC, Ch -3.
5. Prof. Kalai Selvi, MD -- Member
   Prof. of Pharmacology, MMC, Ch -3.
6. Thiru. S. Govindasamy, BA BL -- Lawyer
7. Tmt. Arnold Saulina, MA MSW -- Social Scientist

We approve the proposal to be conducted in its present form.

Sd/ Chairman & Other members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in protocol and patients information / informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003