"A COMPARATIVE STUDY ON CLINICAL EFFICACY OF PLATELET RICH PLASMA IN COMBINATION WITH METHOTREXATE VERSUS METHOTREXATE MONOTHERAPY VERSUS CONVENTIONAL TOPICAL THERAPY IN CHRONIC PLAQUE PSORIASIS"

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In Partial fulfillment of the University regulations for

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THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY,

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CERTIFICATE

This is to certify that the dissertation titled **"A COMPARATIVE STUDY ON CLINICAL EFFICACY OF PLATELET RICH PLASMA IN COMBINATION WITH METHOTREXATE VERSUS METHOTREXATE MONOTHERAPY VERSUS CONVENTIONAL TOPICAL THERAPY IN CHRONIC PLAQUE PSORIASIS"** is a bonafide work done by **Dr. YUVA PRIYA. B,** Post graduate student of the Department of Dermatology, Venereology and Leprosy, Madras Medical College, Chennai - 3, during the academic year 2019 – 2022. This work has not previously formed the basis for the award of any degree.

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DECLARATION

The dissertation entitled **"A COMPARATIVE STUDY ON CLINICAL EFFICACY OF PLATELET RICH PLASMA IN COMBINATION WITH METHOTREXATE VERSUS METHOTREXATE MONOTHERAPY VERSUS CONVENTIONAL TOPICAL THERAPY IN CHRONIC PLAQUE PSORIASIS"** is a bonafide work done by **Dr. YUVA PRIYA. B** at Department of Dermatology, Venereology and Leprosy, Madras Medical College, Chennai-3, during the academic year 2019-2022 under the guidance of **Dr. RAJKUMAR KANNAN, M.D.D.V.L., D.D.V.L.,** Associate Professor of Dermatology, Madras Medical College, Chennai -3.

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I, **Dr. YUVA PRIYA. B** (Reg no : **201930027)** solemnly declare that this dissertation titled **"A COMPARATIVE STUDY ON CLINICAL EFFICACY OF PLATELET RICH PLASMA IN COMBINATION WITH METHOTREXATE VERSUS METHOTREXATE MONOTHERAPY VERSUS CONVENTIONAL TOPICAL THERAPY IN CHRONIC PLAQUE PSORIASIS"** is a bonafide work done by me at Madras Medical College during 2019-2022 under the guidance and supervision of **Dr. RAJKUMAR KANNNAN, M.D.D.V.L., D.D.V.L.,** Associate Professor, Department of Dermatology, Madras Medical College, Chennai-600003.

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Introduction

INTRODUCTION

Psoriasis is a chronic inflammatory, non-communicable disease that predominantly involves skin, nails, joints and associated with systemic manifestations in many organs. The World Health Organization noted that the reported prevalence of psoriasis worldwide ranges between 0.09% to 11.43%, making psoriasis a serious global health problem with at least 100 million individuals affected all over the world. Psoriasis, an inflammatory dermatosis is marked by elevated levels of active phosphorylated NFκB which is the key regulator element in inflammatory pathway, apoptosis, in cellular proliferation and differentiation. Psoriasis is associated with significant negative impact on patient's physical and mental health. Psoriatic patients are at higher risk of developing cardiovascular disorders and associated with multitude of psychological impairment and also have an increased rate of suicidal ideation. The management of psoriasis has witnessed an immediate need for new treatment modality as up to 50% of patients are not content with present therapy.

The common systemic agents such as methotrexate, acitretine and cyclosporine are associated with end organ toxicities and treatment related side effects. Biological agents have the drawback of added cost to the care and iatrogenic immunosuppression. Combinational modality of treatment and intralesional route of drug delivery may potentiate the treatment outcomes and diminish the systemic toxicity.

Intralesional methotrexate produces the higher concentration of the drug at the site of action, while avoiding the complications of systemic therapy and provides an effective and safe method of treating psoriasis. Autologous platelet rich plasma (PRP) has been a breakthrough in stimulation and acceleration of soft tissue healing and used as treatment for several ailments with promising results. HGF (Hepatocyte Growth Factor) is known to function as an anti- inflammatory agent and it's action is primarily mediated by the disruption of transcription factor NFκB signalling which is a crucial regulator of inflammation in psoriasis. Hence PRP might be effective as an adjuvant anti-inflammatory agent and due to it's autologous nature would provide a risk free combination modality to manage psoriatic lesions.

This study was ventured to compare the efficacy of platelet rich plasma in combination with methotrexate, methotrexate monotherapy and conventional topical therapy in the treatment of chronic plaque psoriasis.

Review of Literature

REVIEW OF LITERATURE

Psoriasis is a chronic, inflammatory proliferative skin condition in which both genetic and environmental factors influence. It is characterized by red, scaly and sharply demarcated indurated plaques which present mainly over the extensor surfaces of extremities and scalp. The annual incidence of psoriasis in adults has been reported as between 0.08 and 0.23% [1]. Psoriasis appears to be more common in countries that are further away from the equator and in white people [2]. There are two peak ages of incidence, the first peak occurring between 16 and 22 years and the second peak between 57 and 62 years of age. Studies assessing the use of systemic and biological treatment in cohorts of patients with severe disease report consistently that men are twice as likely to receive systemic therapy as women, suggesting that men may have more severe disease [3].

CLASSIFICATION OF PSORIASIS:

Clinical forms of psoriasis (based on morphology or natural history)

- Plaque psoriasis (psoriasis vulgaris)
- Acute guttate psoriasis
- Unstable psoriasis
- Erythrodermic psoriasis
- Pustular psoriasis
- Atypical forms of psoriasis

Other specified forms of psoriasis (based on age or precipitants):

- Linear and segmental psoriasis
- Psoriasis in childhood and old age
- Photoaggravated psoriasis
- Drug-induced or exacerbated psoriasis
- HIV-induced or exacerbated psoriasis

Psoriasis affecting specific sites:

- Scalp psoriasis
- Follicular psoriasis
- Seborrhoeic psoriasis (sebopsoriasis)
- Flexural psoriasis (inverse psoriasis)
- Genital psoriasis
- Non-pustular palmoplantar psoriasis
- Nail psoriasis
- Mucosal lesions
- Ocular lesions

ETIOLOGY:

The two main factors which influence the psoriasis pathogenesis are

i. Genetic factors

ii. Environmental factors

Genetic factors:

Type I psoriasis is hereditary, strongly associated with HLA-C:06:02), early onset and more likely to be severe. Type II is sporadic, HLA unrelated, of late onset and often mild. Classical genome-wide linkage analysis in pedigrees multiply affected by psoriasis has identified at least 9 chromosomal loci with statistically significant evidence for linkage (PSORS1 – PSORS9) [4]. PSORS1 is located in the major histocompatibility complex (MHC) on chromosome 6p, with a span of approximately 300-kb segment within the class I region [5,6]. Phenotypic variants of psoriasis are genetically heterogeneous at this level of PSORS1. Thus, guttate psoriasis is strongly associated with PSORS1, whereas late-onset (>50 years of age) chronic plaque psoriasis is not. PSORS2 is located within chromosome 17q and it encodes CARD14 gene. Heterozygous gain of- function mutations in CARD14 lead to nuclear factor kappa light chain enhancer of activated B cell (NF-κB) activation in affected keratinocytes and consequent production of cytokines, chemokines and recruitment of inflammatory cells in psoriasis [7,8].

Environmental factors:

1. Infections: Psoriasis can be triggered by streptococcal infection like tonsillitis, particularly guttate psoriasis but also plaque psoriasis. Oligoclonal expansion of T cells occurs in the tonsils in response to streptococcal infection and the same T-cell receptor is found in the peripheral blood and skin of psoriasis patients. Streptococci are facultative intracellular bacteria and are not eliminated by conventional antibiotic therapy, which may explain the lack of efficacy of

antibiotics in treating guttate psoriasis. Tonsillectomy appears to be effective management in some patients [9]. HIV infection can lead to exacerbation of psoriasis.

2. Medications: The most important medications that may exacerbate psoriasis are lithium salts, interferon α, TNF-α inhibitors and synthetic antimalarials. Beta-blockers, non-steroidal anti-inflammatory drugs (NSAIDs) and angiotensin-converting enzyme (ACE) inhibitors have also been implicated. Although psoriasis may respond to corticosteroids, both tachyphylaxis and rebound phenomena can occur. Withdrawal of corticosteroids may lead to rebound of the illness and the development of unstable psoriasis, hence withdrawal should be by steady dose reduction rather than abrupt termination. Patients who smoke cigarettes are at increased risk of developing psoriasis, of having more severe disease and of developing psoriatic arthritis.

3. Smoking has multiple immunological effects which may contribute to the initiation and persistence of psoriasis. There is a strong association between cigarette smoking and palmoplantar pustulosis particularly.

4. Psychological distress: There is a complex relationship between psoriasis and psychological distress. There are numerous anatomical and physiological interconnections between the nervous system and the skin known as the ‘neurocutaneous axis’. These include substance P, calcitonin gene related peptide, corticotrophin releasing hormone and nerve growth factor. Combined with the increased numbers of sensory nerve fibers in psoriasis plaques and the

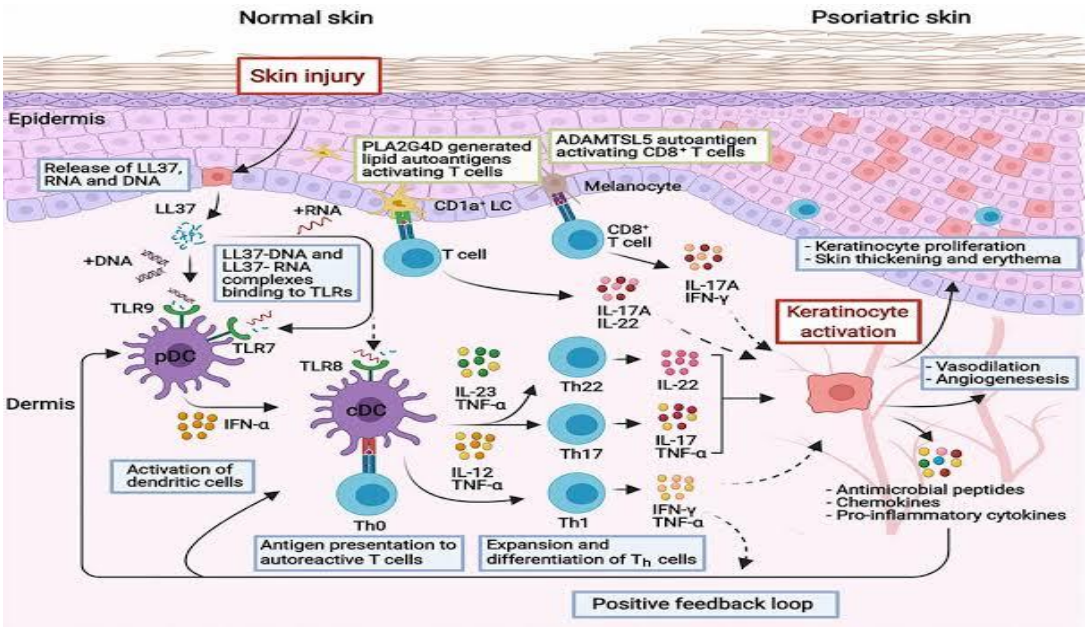
above mentioned neurotransmitters have immune modulatory properties and may play a role in the maintenance of psoriatic plaques [10].

5. Physical trauma: Psoriasis can occur in sites of cutaneous trauma and old scars, so-called Koebner phenomenon and it is proposed that trauma can initiate innate immune activation with subsequent specific immune activation and keratinocyte hyper proliferation and angiogenesis. Up to 25% of patients report the development of new psoriatic lesions in sites of skin trauma and this is common in patients who are HLA-C:06:02 positive [11].

PATHOGENESIS:

Normal basal keratinocytes proliferate, differentiate and ascend through the upper epidermal layers before undergoing senescence and entering the keratin layer. This process takes approximately 30 days in healthy skin. In psoriatic plaques, there is hyper proliferation of the basal layer with subsequent rapid progression through the upper epidermal layers and decreased differentiation [12]. The rete ridges are elongated, there is regular acanthosis and absence of the granular layer. The progression of the basal cell keratinocytes through the entire epidermis takes only 4–5 days in active plaques [13,14]. It is worth noting that clinically normal skin in psoriasis patients has abnormal epidermal dynamics. Cells of the innate immune system like macrophages, neutrophils, mast cells, plasmacytoid dendritic cells and natural killer cells are present in significantly larger numbers in psoriatic skin [15]. The classic immunological response to viral infections and intracellular bacteria include Th1 and Th17 cytokines and the

presence of CD8+ T cells but the langerhan cell migration in response to TNF alpha is impaired [16]. Psoriasis may result from the inappropriate persistent activation of inflammation in response to commensals or to other triggering factors. Injury or infection of the skin results in antimicrobial peptide production and increased Toll-like receptor activation. The antimicrobial peptide like LL-37 (cathelicidin) binds to self-DNA, enabling binding to and activation of Toll-like receptor 9 and induction of interferon-α production by plasmacytoid dendritic cells. LL-37 also binds to self-RNA inducing myeloid dendritic cells to produce TNF-α, IL-23 and IL-6 [17, 18]. It results in activation of T cells of the adaptive immune system, specifically Th17 cells, which in turn activate keratinocytes to proliferate and produce multiple cytokines and antimicrobial peptides [19,20]. Activated T cells are of Th1, Th17 and Th22 phenotype, with a dearth of Th2 cells. In psoriasis plaques there are increased levels of IL-2, IL-8, interferon-γ, TNF-α, IL-15, IL-17, IL-22 and IL-23 [21,22]. There is a distinct absence of Th2 cytokines such as IL-4 and IL-10 [23] (FIGURE 1).



CLINICAL FEATURES:

Chronic plaque psoriasis is the most common variant of psoriasis vulgaris and it is characterized by sharply demarcated and erythematous papulosquamous lesions. Less often, nearly all of the body surface is involved (erythrodermic psoriasis) or numerous, small, widely distributed papules and plaques are seen (guttate psoriasis). Occasionally, there are obvious macroscopic pustules, as in generalized pustular psoriasis or pustulosis of the palms and soles [24]. The configuration of psoriatic lesions due to the Koebner phenomenon reflects the etiology of the trauma. In addition to their characteristic sharp demarcation, psoriatic lesions are sometimes surrounded by a pale blanching ring, which is referred to as woronoff's ring. The classic findings of erythema, thickening and scale are reflections of the histopathological features of elongated dilated capillaries that are close to the skin surface, epidermal acanthosis with cellular infiltrates and abnormal keratinization, respectively. If the superficial silvery white micaceous scales are removed, then a wet surface is seen with characteristic pinpoint bleeding. This finding is called Auspitz sign and it is the clinical reflection of elongated vessels in the dermal papillae with thinning of the suprapapillary epidermis. During exacerbations, psoriatic lesions often itch. Pinpoint papules surrounding existing psoriatic lesions indicate that the patient is in an unstable phase of the illness. In addition, expanding psoriatic plaques are characterized by an active edge with a more intense erythema. The involution of a lesion usually starts in the center, resulting in annular psoriatic lesions. In chronic plaque psoriasis, there is a relatively symmetrical distribution of sharply defined,

erythematous and scaly plaques. Scalp, knees, elbows and lumbosacral area are the sites of predilection and the genitalia are involved in up to 45% of patients. Plaques may persist for months to years at the same locations. Although the course of this disease is chronic, periods of complete remission do occur and remissions of 5 years have been reported in ~15% of patients [25]. Because the percentage of body surface area involved does not reflect the severity of the individual lesions with respect to erythema, induration and scaling, the Psoriasis Area and Severity Index (PASI) was formulated (Table 1). This is a single calculated score that is based on the body surface area involved (in each of four anatomic areas – head, upper extremities, trunk and lower extremities) and clinical grading of lesional erythema, induration and scaling in patients with psoriasis.

combined score ranging from 0 to 72 calculated as Psoriasis Area Severity Index (PASI).

	Thickness 0–4	**Scaling 0–4**	**Erythema 0–4**	**× Area 0–6**		**Total**
Head	a	b	c	d (a + b + c)	× 0.1	= A
Upper limbs	e	f	g	h (e + f + g)	× 0.2	= B
Trunk	i	j	k	l (i + j + k)	× 0.3	= C
Lower limbs	m	n	o	p (m + n + o)	× 0.4	= D
					PASI	= A + B + C + D

Severity	0 = none	Area	0 = no involvement	Axillae = upper limb
	1 = mild		1 = 0 <10%	Neck/buttocks = trunk
	2 = moderate		2 = 10 <30%	Genito-femoral = lower limb
	3 = severe		3 = 30 <50%	
	4 = very severe		4 = 50 <70%	
			5 = 70 <90%	
			6 = 90 <100%	

COMPLICATIONS:

Psoriatic arthritis is the most common inflammatory disease associated with psoriasis. Inflammatory bowel disease (IBD) is also more frequently associated [26]. There may be an increased risk of other autoimmune diseases like alopecia areata, vitiligo and urticaria, particularly in psoriatic arthritis. Psoriatic plaques are usually resistant to infection and it is probably in part caused by the overexpression of endogenous antimicrobial peptides like cathelicidins and β-defensins. Occasionally, flexural psoriasis becomes clinically infected, especially if fissuring occurs (e.g. in the natal cleft). In addition to the known effect of streptococcal infection in precipitating disease, patients with psoriasis have been shown to be 10 times more likely to develop pharyngitis than healthy individuals and streptococci are more likely to be isolated in association with a sore throat [27]. Psoriasis is associated with significant psychological impairment, including pathological worrying, dysfunctional thought, fear of stigmatization, effects on self-image, personality and temperament. Excessive alcohol consumption has been found significantly more common in men with severe psoriasis and could be a consequence of stress caused by psoriasis. There are reports of an association between various non-melanoma skin cancer and psoriasis, which could be due to high-dose of PUVA, and also compounded by immunosuppressive treatments like ciclosporin, methotrexate, TNF-α inhibitors and possibly high-dose UVB. There is some evidence for a modestly increased risk in psoriasis of systemic lymphoma, particularly Hodgkin lymphoma. Psoriasis significantly increases the risk of stroke and myocardial infarction [28]. The risk appears to be more in younger patients than with more severe disease or with psoriatic arthritis. There is also an

increased risk of peripheral vascular disease, venous thromboembolism and atrial fibrillation [29]. The increased vascular risk probably relates to behaviours like cigarette smoking, which is more frequent amongst those with psoriasis and traditional cardiovascular risk factors like metabolic syndrome [30]. Psoriatic patients are at higher risk of developing metabolic syndrome including obesity, dyslipidemia, diabetes, hypertension and more recently atherosclerosis [31]. Systemic inflammation plays a significant role in the pathogenesis of atherosclerosis in psoriasis patients. Therefore, persistent skin inflammation in psoriasis patients may contribute to the development of premature atherosclerosis [32]. In addition, systemic treatment of psoriasis with methotrexate or TNF-α inhibitors may be associated with reduced frequency of cardiovascular events [33]. Death rates due to liver impairment have been reported to be significantly elevated in psoriatic patients. Non-alcoholic fatty liver disease is the most frequently identified liver disease, present in up to 50% of patients with psoriasis. It is associated with more severe psoriasis, obesity and metabolic syndrome. Neutrophilic cholangitis is an important cause of liver dysfunction in patients with generalized pustular psoriasis and occasionally in chronic plaque psoriasis. Rarely secondary amyloidosis has occasionally been reported, which could be due to immunoglobulin A (IgA) nephropathy [34,35]. Psoriasis is also associated with an increased risk of gout and hyperuricaemia. Pregnancy outcomes in patients with mild psoriasis appear to be unaltered, but in severe disease a higher prevalence of adverse outcomes like spontaneous abortion, pre-eclampsia and low birth weight have been reported.

DISEASE COURSE AND PROGNOSIS:

In many instances, plaque psoriasis is chronic and persistent. In some individuals, the disease is less stable with considerable variation in the extent and degree of inflammation, which could be due to environmental triggers such as infections, alcohol consumption, emotional stress or winter. In the few longitudinal studies that have been done, spontaneous remission occurs in between a third and a half of patients and has been reported for as long as 54 years. Guttate psoriasis carries a better prognosis than those of a insidious and more diffuse onset and have longer remissions after treatment. In the contrary, erythrodermic and pustular forms carry an appreciable mortality and psoriatic arthritis has a considerable morbidity. It is now known that severe chronic plaque psoriasis will also appreciably shorten life expectancy by an average of 4–6 years.

INVESTIGATIONS:

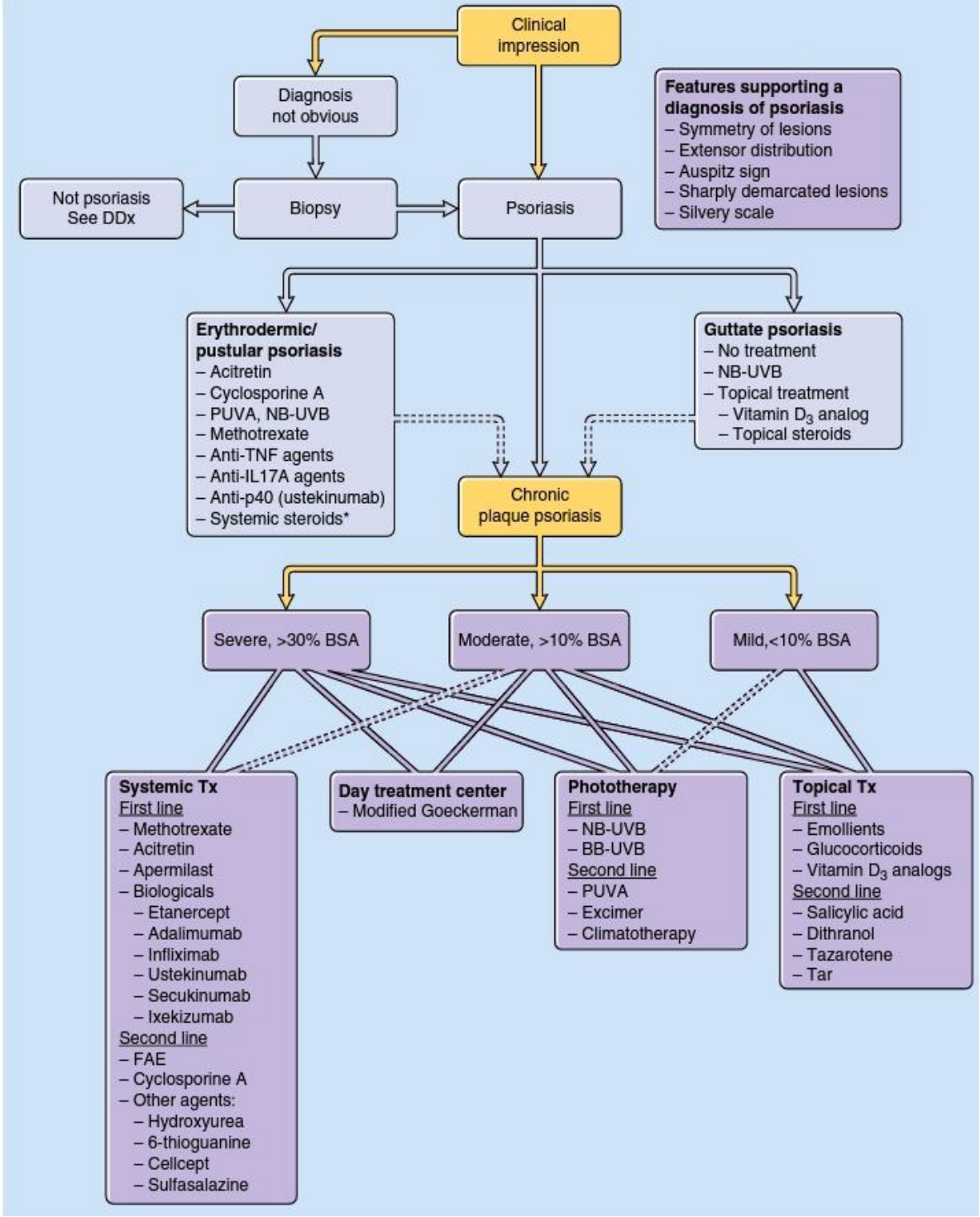
The diagnosis of psoriasis is usually clinical. A skin biopsy of lesional skin may occasionally be helpful in atypical presentations. High sensitivity C-reactive protein may be slightly elevated, with higher levels seen in psoriatic arthritis and generalized pustular psoriasis. Investigations appropriate for initiating or monitoring of biological and systemic treatments may be required. Screening for associated co-morbidities should also be done which will include assessments for psoriatic arthritis, metabolic syndrome and depression.

MANAGEMENT:

A broad spectrum of topical and systemic antipsoriatic treatments is available for the management of psoriasis. But in most treatments, the duration of a treatment is restricted because of the cumulative toxicity of an individual treatment, and in some instances, treatment efficacy may diminish with time. Some treatments, such as methotrexate, calcipotriol, and acitretin, can be regarded as appropriate for continuous long term use [36]. These treatments maintain high efficacy and have low cumulative toxicity. In contrast, topical corticosteroids, tar, dithranol, phototherapy and cyclosporine are not indicated for continuous chronic use, and rotational or combinational treatments are suggested [37]. Patients with stable chronic plaque psoriasis who respond well to topical treatments may not require a change of treatment. In cases of itchy/pruritic psoriasis, treatments with an irritant effects, such as dithranol, vitamin D3 analogs, and phototherapy, should be used cautiously, whereas treatments with potent anti-inflammatory effects, such as topical corticosteroids should be used more appropriately. In patients with erythrodermic and pustular psoriasis, short course of cyclosporine, acitretin and methotrexate are the drug of choice and treatments with an irritant potential should be avoided.

FIGURE 2 is an algorithm showing recommended treatments for various forms of psoriasis.

Diagnosis and treatment algorithm for patients with psoriasis



TOPICAL TREATMENT:

Most cases of psoriasis are treated topically. In most cases, ointment formulations are more effective than creams but are less cosmetically acceptable and time consuming to use. For many patients, it is worth prescribing both ointment and cream formulations; cream for use in the daytime and ointment for night time. Topical agents are also used adjunctively in patients who are concurrently being treated with either phototherapy or systemic agents and for resistant lesions in patients with extensive psoriasis. The management of psoriasis is individualized with consideration of the extent of the disease and its consequences on the patient's quality of life as well as the likely benefits and potential adverse effects of specific treatments. Corticosteroids since their introduction from 1950, topical corticosteroids have become a conventional and mainstay in the treatment of psoriasis [38]. They are first-line therapy in mild to moderate psoriasis. Corticosteroids are available in various vehicles, from ointments, creams gel, lotions, shampoos, foams and sprays. Among that ointment formulations have the highest efficacy. By increasing lipophilicity of corticosteroids via masking of hydrophilic 16- or 17-hydroxy groups or by introducing propionates, acetonides or valerates, their anti-inflammatory properties have been significantly improved. Application under hydrocolloid or plastic occlusion also enhances the penetration. Once-daily application has been shown to be as effective as twice-daily application, and long-term remissions may be maintained by applications on alternate days. The maximum improvement is usually achieved within 2 weeks and remission is maintained with maintenance

therapy consisting of 12 weeks of intermittent applications of corticosteroid ointment. As tachyphylaxis or rebound phenomena can occur within a few days to weeks, intermittent treatment schedules like once every 2 or 3 days or on weekends, are advised for more prolonged treatment courses. Combination topical therapy can take advantage of rapid effect of topical corticosteroids and the prolonged benefits of long-term treatment with topical agents like vitamin D3 analogues or salicylic acid [39,40].

HALOBETASOL PROPIONATE:

Topical potent corticosteroids plays an important role in psoriasis treatment. Halobetasol propionate is a superpotent topical corticosteroid. The structure of halobetasol propionate is 21-chloro- 6α, 9-difluoro- 11β, 17-dihydroxy-16β- methylpregna- 1,4- diene-3-20-dione, 17-propionate. It has the following structural formula (FIGURE 3).

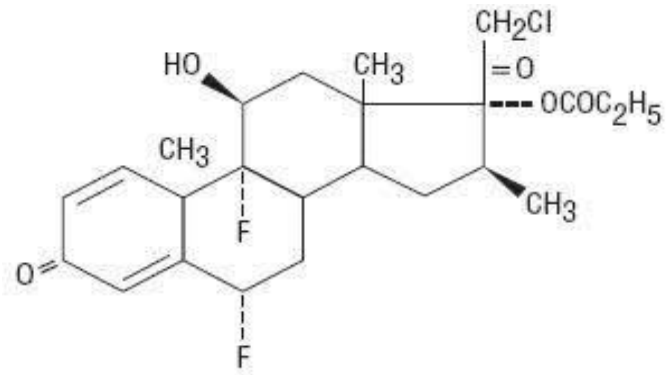


Figure 3

The state of the epidermal barrier, lipophilicity of drug and additional double bond at 1,2 position are some of the factors affecting the potency of topical corticosteroids. Based upon the effect of transient vasoconstriction produced by

topical corticosteroids, Halobetasol propionate is classified under super potent category.

Mechanism of action: Corticosteroids mediate its action by acting on Glucocorticoid Receptors(GR) [41]. Glucocorticoid receptors can be GRα or GRβ. At the cellular level, corticosteroid acts on GRα receptor in two different pathways which can be 15 either genomic or non-genomic (FIGURE 4). GRβ which is receptor in cytoplasm, acts as an endogenous inhibitor of glucocorticoid action [42]. This receptor is up regulated by stapylococcal superantigens [43]. **(Figure 4)**

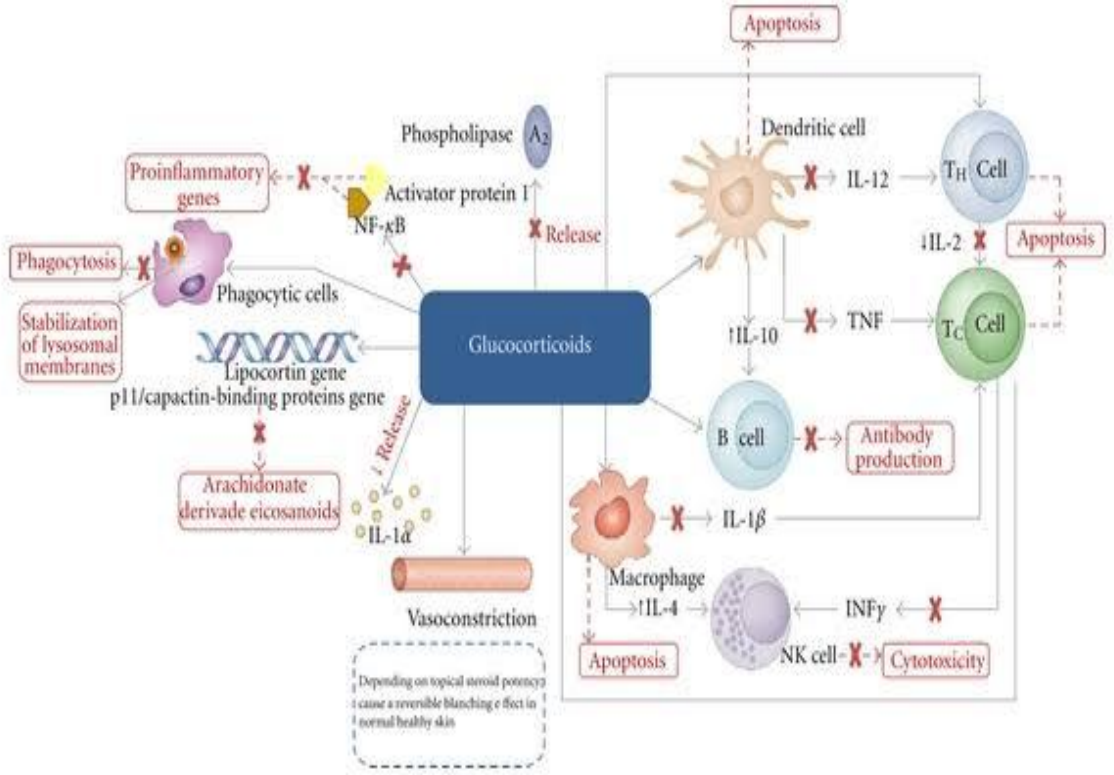


Figure 4

In the genomic pathway, Corticosteroid molecules diffuse into the target cell, binds to Glucocorticoid Receptor (GRα) in the cytoplasm. This complex undergoes various conformational changes and diffuse into nuclear envelope and binds to the Glucocorticoid Response Elements(GRE) in the DNA resulting in transcription and regulation of various anti inflammatory genes like phosphoenol pyruvate carboxy kinase, tyrosine amino transferase, IL-10 and IL-1 receptor antagonist. Corticosteroids causes transrepression of multiple proinflammatory genes like nitric oxide, growth factors, adhesion molecules, prostanoids and other autocoids [44]. It also acts through nuclear factor-κB leading to its transrepression which requires lower cortisol levels than that required for other mechanism. In the non-genomic pathway, corticosteroids bind to the receptors which are located on the cellular membrane. It stabilize the cell and lysosomal membranes and prevent the release of lysosomal contents and phospholipid precursors for prostaglandin synthesis. It has antiinflammatory, antiproliferative, apoptotic, immuno-modulatory and vasoconstrictive act [45].

Anti-inflammatory Effect:

Corticosteroids induces Annexin A1 or Lipocortin 1 expression. It is found in the cytoplasm of basal keratinocytes of normal skin. In psoriasis, it is translocated to the cell membrane in which it binds to phospholipids thereby reducing inflammatory prostanoids level. Annexin A1 also inhibits phospholipase A2 thereby inhibiting the synthesis of leukotrienes and prostaglandins. It also stabilizes lysosomal membrane and prevents the release of prostaglandin

precursors. It reduces chemotaxis, phagocytosis in neutrophils and activation of lymphocytes in response to macrophage activating factor. It reduces the production of interleukin-1 (both IL-1α andIL-1β), tumor necrosis factor, IL-2, IL-3 IL-6, interferon-γ, TNF alpha, IL-8, RANTES, eotaxin and granulocyte–monocyte colony-stimulating factor. It also induces the expression of MAPK phosphatase 1 which inactivates C-Jun and the terminal kinase in MAPK pathway leading to antiinflammatory effect [46]. The resistance of some inflammatory disease to corticosteroids can be due to defects in the expression of MAPK phosphatase. Corticosteroids also inhibit the enzyme iNOS, thereby inhibiting the nitric oxide production in psoriatic skin. The inhibition of mast cell degranulation by corticosteroids prevents the release of pro inflammatory mediators also [47].

Anti-proliferative effect:

As it inhibits the Keratinocyte Growth Factor (KGF), mitotic activity of keratinocyte is diminished and there is reduction in the thickness of stratum corneum, granular layer is absent and flattening of basal layer of keratinocytes. Melanocytes pigment production is also inhibited. Ultrastructure of keratinocytes and basement membrane are unaffected. In the dermis, it inhibits fibroblast proliferation and reduces dermal volume by causing reduction in Glycosaminoglycans. It also causes vasoconstriction. The late changes include reduction of collagen and elastic fibers with abnormal aggregation and it also causes fragility of dermal vessels [48].

Anti apoptotic properties:

Corticosteroids decrease the survival rate of both lymphocytes and eosinophils by blocking the IL-5 and GM-CSF. On the contrary, it reduces the apoptosis and enhance the survival of polymorphonuclear cells [49].

Vasoconstrictive properties:

The potency of the topical corticosteroids is estimated by vasoconstrictive properties of corticosteroids. It could be due to blocking of action of vasodilators like histamine and bradykinin [50].

TOPICAL CORTICOSTEROIDS USES:

1. ATOPIC DERMATITIS

TCS are first-line treatments for atopic dermatitis in all age groups and their efficacy is well established in randomized, controlled clinical trials. For adults, moderate-potency TCS are used for flares on the trunk and extremities; typically, control of the disease occurs after 2–3 weeks of twice-daily therapy. To finish treatment or to treat early recurrences, a lower potency of the TCS can be used twice daily. Fluticasone propionate 0.05% cream applied once daily was as effective as twice-daily treatment. Prophylactic treatment with mometasone furoate cream twice weekly for 6 months is also effective.

For children with atopic dermatitis, lower-potency TCS are recommended. Twice-daily desonide hydrogel 0.05%, flucocinolone acetonide 0.01% in peanut oil, hydrocortisone butyrate 0.1% lipocream and once-daily fluticasone

proprionate 0.05% lotion have been shown to be effective and safe for up to 1 month in children down to 3 months of age. Occasionally, intermediate-potency TCS are necessary for very short courses.

Compliance with TCS may be a very significant issue in atopic dermatitis patients. Adherence to regimens varies significantly, though patients may report near perfect usage.

Ceramide-based barrier creams, pimecrolimus cream and tacrolimus can augment the benefit of TCS therapy of atopic dermatitis in both adults and children.

2. DISCOID LUPUS ERYTHEMATOSUS

Fluocinonide 0.05% cream and topical tacrolimus 0.3% in clobetasol propionate 0.05% ointment, have shown to be effective in treating individuals with discoid lupus erythematosus.

3. GRANULOMA ANNULARE

Superpotent TCS alone or high-potency TCS under occlusion are effective treatments for localized granuloma annulare. Occlusive TCS preparations (such as Cordran tape) and intralesional TCS treatment (such as 5–10 mg/ mL triamcinolone acetonide) are also effective.

4. LICHEN PLANUS

Localized cutaneous lichen planus generally responds to TCS. Oral erosive LP can be effectively treated with TCS in gels, ointments, sprays and

rinses. Dexamethasone elixir (in generic form) and prednisone oral solution (Orapred) rinses are currently available. Mometasone furoate 1% microemulsion mouthwash three times daily over 30 days also can reduce pain and lesion surface area. Fluticasone propionate spray four times daily and betamethasone sodium phosphate mouth rinse four times daily were can also be used. TCS are also useful in the treatment of lichen planopilaris.

5. LICHEN SCLEROSUS ET ATROPHICUS

Lichen sclerosus et atrophicus can be effectively treated with TCS. A regimen of high-potency or superpotent TCS, followed by maintenance with low-potency TCS is found to be very effective.

6. PSORIASIS – GENERAL APPROACH

TCS are most useful for localized psoriasis or psoriasis of the scalp. Localized plaque psoriasis generally requires a high-potency or superpotent TCS twice daily, followed by a maintenance regimen, to obtain and preserve remission. Efficacy rates are variable between and within the different classes of TCS. Twice-daily clobetasol propionate 0.05% ointment is the most preferred regimen. The recommended (short-term) therapy for inverse psoriasis is low- to mid-potency TCS. For childhood psoriasis, calcipotriene with or without TCS can be used.

PSORIASIS – SCALP TREATMENT

TCS are the recommended (short-term or intermittent) therapy for scalp psoriasis. Many physicians treat thick psoriatic plaques on the scalp with a high-

potency or superpotent TCS solution or foam nightly to twice daily, 2 weeks on and 1 week off, combined with the daily am use of a therapeutic shampoo containing coal tar or salicylic acid. Short-contact treatment with clobetasol-17 propionate 0.05% shampoo once daily for 4 weeks can also be used.

7. PSORIASIS – COMBINATION OF TCS WITH VITAMIN D PRODUCTS

The success of topical calcipotriene (calcipotriol) alone and in combination regimens with TCS has led to the development of single-agent, combination products. A fixed combination ointment of calciptriol and betamethasone dipropionate produced about 80% satisfaction rates in a 1224-patient, multicenter, single-group, non-interventional 6-month study [50].

PSORIASIS – COMBINATION OF TCS WITH OTHER THERAPIES

TCS have been tested for patients with psoriasis in combination with various other therapies such as biologics, phototherapy, systemic therapy, and other topical therapies. Although further research is needed, the addition of clobetasol proprionate 0.05% spray seems an effective and safe add-on therapy to a stable regimen of biologic treatment in patients with moderate to very severe plaque psoriasis. Many studies showed more rapid clearing rates of psoriasis using psoralen plus ultraviolet A (PUVA) plus TCS than with PUVA alone. An intermediate- to high-potency TCS may be used concurrently during PUVA photochemotherapy to achieve a faster rate of clearing, a lower total UVA dose at clearing, and a lower final UVA dose. The combination of TCS with UVB phototherapy appears to have no substantial effect on the time to clearing or the

percentage of responders. TCS have been associated with an increased risk of earlier relapse after the Goeckerman regimen. The addition of TCS leads to more rapid clearing of psoriatic plaques with short-course cyclosporine therapy, although relapse rates remained unchanged. TCS are also beneficial when used with salicylic acid, anthralin, calcipotriene, or tazarotene.

PSORIASIS – EFFECTS OF OCCLUSION

Combining TCS with occlusion can increase efficacy. Triamcinolone acetonide ointment 0.1% is more effective under occlusion than either clobetasol propionate cream 0.05% twice daily or triamcinolone acetonide ointment 0.1% alone. Weekly clobetasol lotion applied under occlusion with a hydrocolloid dressing demonstrated excellent results in chronic plaque psoriasis, psoriasis of the palms and soles, palmoplantar pustulosis, and in skin lesions of Reiter's disease. Hydrocolloid-occluded clobetasol propionate lotion once weekly induced a faster remission of localized psoriasis than did unoccluded clobetasol propionate ointment twice daily.

8. SEBORRHEIC DERMATITIS

Only low-potency TCS creams are necessary for control of seborrheic dermatitis on the face. If traditional antidandruff shampoos fail, moderate- to high-potency TCS lotions or solutions may be used on the scalp. Physicians frequently use Alcortin (iodoquinol 1% and hydrocortisone 2%) gel twice daily, 2 weeks on and 1 week off, as needed, for the face, and 0.01% fluocinolone acetonide solution nightly for the scalp.

9. WELL'S SYNDROME

TCS successfully treats initial or subsequent episodes of eosinophilic cellulitis.

10. BULLOUS DERMATOSES

The mucous membrane lesions of vesiculobullous disorders, such as pemphigus vulgaris, can often be treated with TCS preparations. For mild oral PV with no cutaneous involvement, a fluorinated TCS such as fluocinonide 0.05% (in a dental paste, such as Orabase, or a gel) can be applied four times daily (after meals and at bedtime). For moderate oral PV, physicians frequently use dexamethasone elixir 0.5 mg/5 mL one teaspoon to swish, hold in the mouth for a few minutes and then spit, four times daily. After the initial lesions respond, a less potent 0.1% triamcinolone acetonide in a dental paste can be substituted. Epidermal atrophy from TCS is not cosmetically or functionally significant on the oral mucous membranes. Similarly, treatment of mucosal lesions of cicatricial pemphigoid, bullous pemphigoid, or pemphigus foliaceus might respond to TCS alone prescribed as previously described. Paraneoplastic pemphigus lesions are typically refractory to TCS. Treatment of cutaneous bullous pemphigoid (BP) with superpotent TCS has been successful for limited and generalized skin involvement.

11.EROSIVE PUSTULAR DERMATOSIS

Erosive pustular dermatosis of the scalp and non-scalp following cryosurgery, radiotherapy, surgery, incidental trauma and laser therapy has been successfully treated with TCS, although tacrolimus may be an equal alternative.

12.BEHCET'S DISEASE

Treatment of Behçet's disease with TCS is based on anecdotal or open clinical trials. A high-potency or superpotent TCS in an ointment or vehicle such as Orabase should be applied directly to the oral or genital erosions four times daily for 1–2 weeks until resolved.

13.PYODERMA GANGRENOSUM

Application of a superpotent TCS might halt the progression of a very early papular or pustular lesion; however, intralesional or systemic corticosteroids are usually required for more advanced lesions of pyoderma gangrenosum.

14.ALOPECIA AREATA

Treatment of alopecia areata with TCS is based mostly on anecdotal experience and long-term efficacy is unproven. For adults, application of a superpotent TCS preparation in a gel, lotion, or solution base to the patch and 1 cm of adjacent skin twice daily, for 2 weeks on and 1 week off, is recommended for a trial period of 2–3 months. For children, mid-potency TCS are the treatment of choice. TCS are frequently combined with topical minoxidil.

15.PATCH-STAGE CUTANEOUS T-CELL LYMPHOMA

Prospective reviews demonstrate that TCS, especially ultrapotent compounds, are an effective treatment for patch-stage cutaneous T-cell lymphoma.

16.VITILIGO

TCS can be effective repigmenting agents in patients with vitiligo. The recommendations are a mid-to-lower potency TCS cream daily for a 3–4-month. Therapy is continued if repigmentation occurs, but stopped if it does not. A Wood's lamp is useful for monitoring progress at 6-week intervals.

17.MELASMA

TCS can be used as triple combination of once-daily application of fluocinolone acetonide 0.01%, hydroquinone 4%, and tretinoin 0.05% cream in melisma.

18.OTHER DERMATOLOGIC USES

Mometasone furoate twice daily has been shown to be a reasonably good alternative to intralesional steroids as an initial choice for treating superficial hemangioma. A short course of hydrocortisone 1% ointment can be effective for pruritus ani. Aqueous/alcohol TCS lotions have proved useful for the treatment of corticosteroid-responsive peristomal dermatoses where creams and ointments can cause ostomy bag detachment.

SIDE EFFECTS:

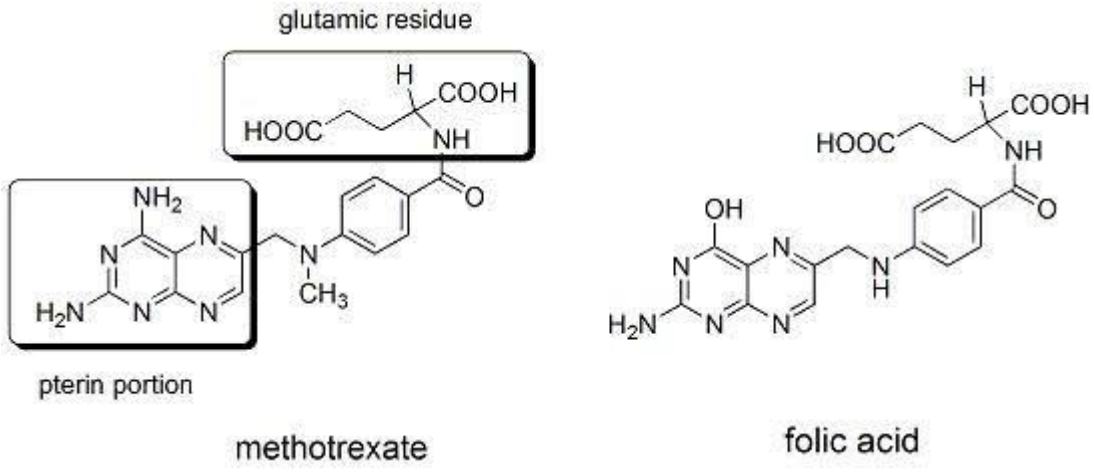
The impaired barrier function in psoriasis and vasodilation in psoriatic vessels leads to more systemic absorption resulting in systemic toxicity.

Topical corticosteroids causes systemic adverse effects like suppression of Hypothalamo-Pituitary axis, cushing syndrome, growth retardation, reinfection with latent virus like cytomegalovirus, osteoporosis, cataract and glaucoma.

Local effects are epidermal atrophy, erythema and telangiectasia leading to rubeosis steroidica, purpura, striae, hypertrichosis, acne, perioral dermatitis and rosacea [51].

METHOTREXATE:

Chemical structure of methotrexate is 4-amino-N 10 methyl pteroylglutamic acid. It is a potent competitive inhibitor (antagonist) of the enzyme dihydrofolate reductase [52]. It is structurally similar to folic acid (FIGURE 5).



Pharmacokinetics:

MTX can be administered orally, intramuscularly, intravenously or subcutaneously. It is well distributed throughout the body except in the brain, penetrating the blood brain barrier poorly. In the plasma, it has a triphasic reduction. The first phase occurs rapidly (0.75h) and reflects distribution of the MTX throughout the body. The second phase of the plasma level reduction is due to renal excretion and it occurs over 2–4 hours. MTX is a weak organic acid excreted mainly through the kidneys. The third phase represents the terminal half-life and varies between 10 and 27 hours. This phase is thought to be due to slow release of MTX from the tissues, primarily bound to dihydrofolate reductase [53]. Approximately 50% of drug is bound to plasma proteins, and the active portion of MTX is the free fraction (unbound) in the plasma. The drug is metabolized intracellularly into polyglutamated forms. These metabolites are also potent inhibitors of dihydrofolate reductase [54].

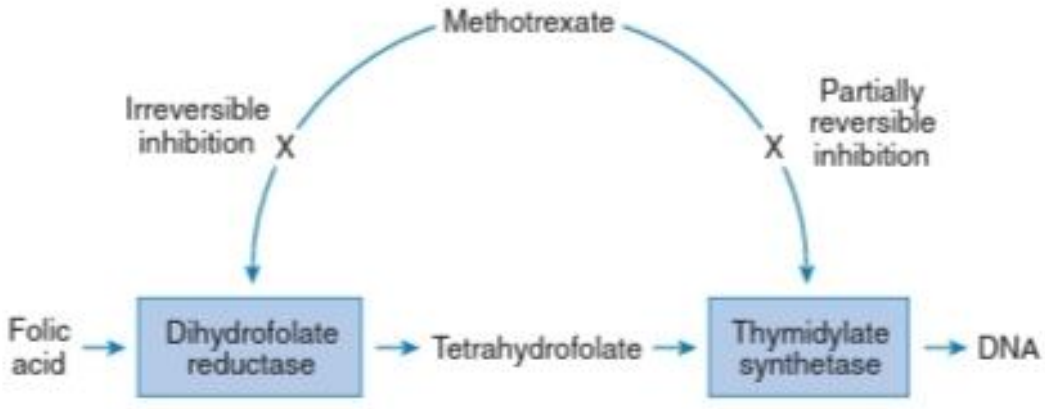


Figure 6

MECHANISM OF ACTION:

Effect on DNA synthesis: MTX reversibly and competitively binds to dihydrofolate reductase within 1 hour of administration, with an affinity greater than that of folic acid. It prevents the conversion of dihydrofolate to tetrahydrofolate as shown in Fig 6. Tetrahydrofolate is a significant co-factor in the production of one carbon units, which are critical for the synthesis of thymidylate and purine nucleotides needed for DNA and RNA synthesis. A partially reversible, but a less rapid competitive inhibition of thymidylate synthetase also occurs within 24 hours of MTX administration. Intra-dermally administered methotrexate inhibits DNA synthesis for 12 to 16 hours in normal as well as in psoriatic skin. Intramuscularly it causes complete inhibition of DNA synthesis in psoriasis but only partial inhibition in normal epidermis. Comparing to the normal skin, psoriatic epidermis is more sensitive to the action of methotrexate. This may be due to increased drug sensitivity of the individual abnormal cell, as well as to increased percentage of psoriatic cells in the methotrexate-susceptible part of S phase of the cell cycle [55].

Anti inflammatory effect:

The anti inflammatory effect is mainly due to the increased production of adenosine which is due to the complex interaction of MTX with AICAR transformylase and ecto 5'nucleotidase (FIGURE 7).

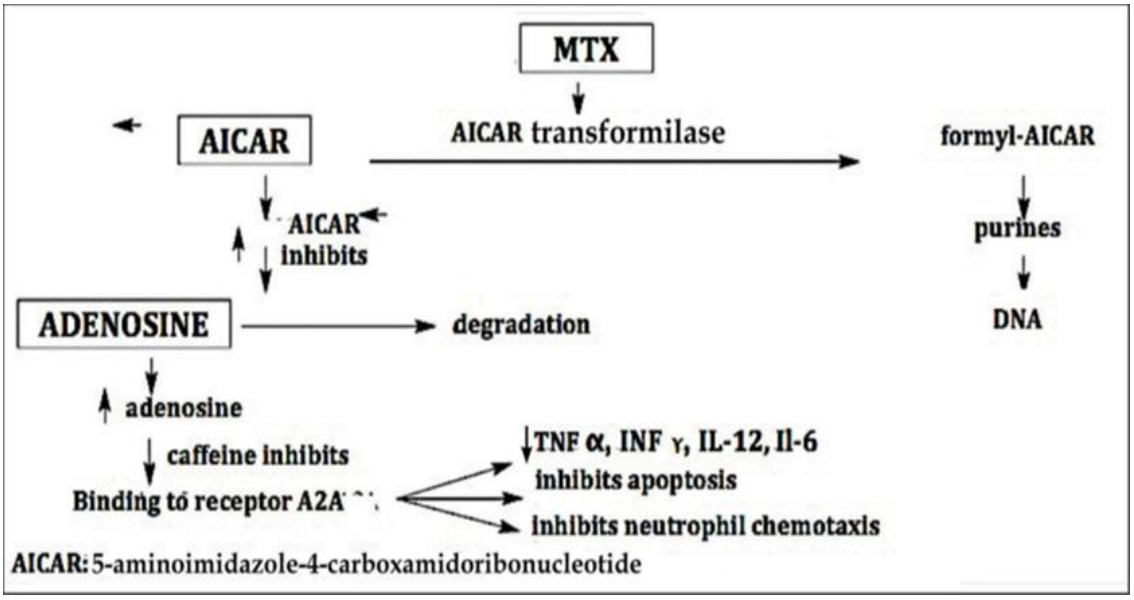


Figure 7

Effects on T cells:

MTX causes reduction in lymphocyte proliferation and also blocks the migration of lymphocytes into the activated tissues by blocking the endothelial E-selectin. Recent evidence suggests that methotrexate works by decreasing the number of circulating CLA+ T cells; reducing inflammatory infiltrate into the dermis and epidermis by down regulating adhesion molecules in endothelial cells and decreasing the expression of adhesion molecules on T cells.

Uses:

- FDA approved indications are Psoriasis and Sezary syndrome [56].
- Other uses are proliferative dermatoses which include Pityriasis rubra pilaris, Reiter's disease and Pityriasis lichenoides et varioliformis acuta.
- Immunobullous dermatoses like Pemphigus vulgaris,Bullous pemphigoid, Cicatricial pemphigoid, Epidermolysis bullosa acquisita.

Autoimmune connective tissue diseases like Systemic sclerosis, Dermatomyositis, Subacute cutaneous lupus erythematosus, Systemic lupus erythematosus, Morphea/localized scleroderma, Scleredema diabeticorum.

Vasculitis includes Leukocytoclastic vasculitis, neutrophilic dermatoses, Cutaneous polyarteritis nodosa, Behcet's disease, Kawasaki disease and Pyoderma gangrenosum.

Other detmatological uses are Keloids, Atopic dermatitis, Sarcoidosis, Lymphomatoid papulosis, Keratoacanthomas, Cutaneous crohns disease, Mycosis fungoides and Chronic idiopathic urticarial [57,58].

In Psoriasis, MTX is indicated for moderate to severe forms of chronic plaque psoriasis, nail psoriasis, psoriatic erythroderma, Palmoplantar pustulosis, generalized pustular psoriasis and psoriatic arthritis [59]. It is also indicated in patients who fail to respond with topical therapy, phototherapy or acitretin. It can also be used as a combination therapy with other immunosuppressive agents and biologicals. Methotrexate increases the efficacy of biologicals by inhibiting the formation of antibodies against biological [60].

Topical Methotrexate is used in palmoplantar and localized chronic plaque psoriasis to overcome systemic toxicity. Topical preparations are available in the dose of 0.25, 0.5, 0.1 and 1%. It's penetration is improved by Laurocapram. Niosomal Methotrexate is available as chitosan gel (0.25%), hydrophilic gel 1%.Side effects of topical preparations are redness, irritation, purpura blisters and sensitization.

Intralesional Methotrexate is indicated in localized chronic plaque psoriasis, limited morphea, keratoacanthoma and nail psoriasis. In nail psoriasis, a dose of 2.5 to 5mg/week drug is injected into proximal nail fold and matrix (2.5mg weekly for * 6 weeks or 5mg/week OD monthly* 3 months or 5 sessions 2.5mg/week at 3 weekly interval).

In palmoplantar psoriasis, Methotrexate can be delivered through Iontophoresis if resistant to other topical therapies. Electroporation is a other mode of delivering methotrexate to skin in which an anion lipid enhancer under a mild hyperthermic environment is used for effective drug delivery. In this, systemic toxicity of MTX is reduced.

Systemic therapy of Methotrexate includes single weekly oral, intravenous, intramuscular or subcutaneous administration of 7.5 to 30 mg/week (0.2 to 0.4 mg/kg/week),Intermittent weekly parenteral - intramuscular route max 50 mg/week, Intermittent oral schedule of three divided doses- 2.5 to 5.0 mg at 12-hour intervals for three doses per week.

ADVERSE EFFECTS:

- Adverse effects include hepatotoxicity,
- Pulmonary toxicity- pulmonary fibrosis, acute Pneumonitis [61,62],
- Haematology-pancytopenia, GIT nausea, vomiting,
- Malignancy-Lymphoma, Renal toxicity at high doses, Reproductive-teratogen and abortificient.
- Methotrexate is classified under Pregnancy category X [63].

Other side effects include osteopathy, increases serum homocysteine level. Cutaneous side effects include Radiation recall phenomena with phototherapy / radiotherapy, MTX-Induced Accelerated Rheumatoid Nodulosis, MTX-induced papular skin eruptions (Paradoxical Drug Reaction), Flag sign - hyperpigmented bands on hair, alternating with normal colored hair, alopecia - telogen effluvium, anagen alopecia, urticaria, local epidermic necrosis, vasculitis, Anaphylactic reaction, Macular erythema (capillaritis), TEN and Ulcerative stomatitis [64,65].

Methotrexate resistance is mediated by mutation in Reduced Folate Carrier (RFC), Multidrug Resistance Protein Family (MRP) or DHFR gene.

PLATLET RICH PLASMA:

- Concept of PRP started in the field of hematology in 1970's
- Initially used to treat thrombocytopenia
- In the late 1990's –in oral and maxillofacial surgeries [66]
- Later due to its versatile anti‑inflammatory and immune modulatory actions, PRP found wide interest in a variety of clinical fields, including dentistry and ophthalmology. Use of PRP is of interest particularly among orthopedicians and sports medicine experts due to its regenerative and tissue healing effects [67]. Moreover, PRP has found use in Dermatology, in conditions such as alopecia, wound healing, and skin rejuvenation.

Definition:

PRP (also called platelet concentrated plasma or platelet rich growth factors), is a biological product which is a portion of plasma fraction of autologous blood with a platelet concentration above the baseline and multiple growth factors.

Growth factors help in modulation of tissue repair and regeneration

Plasma proteins acts as a scaffold for bone, connective tissue and epithelial migration. PRP continues to evolve as an important treatment modality with many applications in Dermatology, particularly in skin rejuvenation, acne scars, dermal augmentation and striae distensae. Furthermore, combining PRP with LASERS, dermal fillers, microneedling and autologous fat transfer produces synergistic effects, leading to enhanced aesthetic results [68].

Concentration of PRP:

- Normal baseline value of platelets count of whole blood is 1-4 lakhs/µl
- PRP with platelet counts of >10 lakhs/µl (4-6 times the baseline) is considered an effective concentration [69].

Classification of PRP:

Based on leukocyte and fibrin content the PRP is classified into

i. P-PRP,

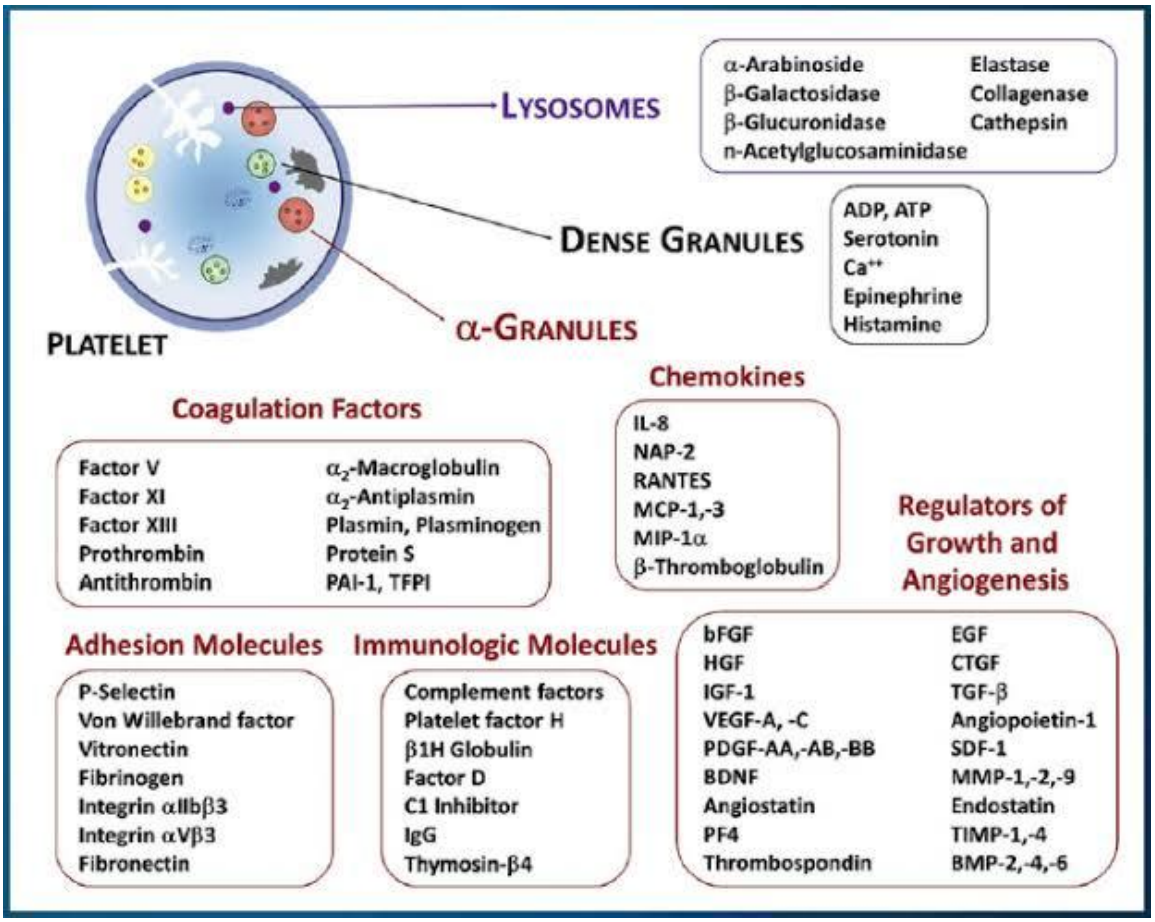
ii. L-PRP,

iii. P-PRF,

iv. L-PRF

COMPOSITION OF PRP:

PRP is an autologous blood product containing a rich concentration of not only platelets, but a variety of growth factors, chemokines, cytokines and proteins. This unique power packed composition of growth factors not only produces tissue repair, regeneration, anti inflammatory and alters angiogenesis but also plays a significant role in connective tissue remodelling and cell cycle regulation [70]. The key growth factors present in PRP are summarized in FIGURE 8.



PRP PREPARATION:

PRP was prepared as follows

- Obtain whole blood of about 5-6ml in sodium citrate containing blue tubes
- Centrifuge blood using a ‘soft’ spin at 2000rpm for 8 minutes
- Transfer supernatant plasma containing platelets into another sterile tube without anticoagulant(red tube)
- Centrifuge the tube at a higher speed (a hard spin) at 4000rpm for 10 minutes to obtain a platelet concentrate
- Lower 1/3rd is PRP and upper 2/3rd is platelet-poor plasma (PPP)
- At bottom of the tube, platelet pellets are formed
- Discard PPP (upper 2/3rd) and mix the PRP (lower 1/3rd) with the pellets by gently shaking tube
- Do not chill blood at any time before or during platelet separation
- Contain platelet concentrations higher than those normally found in circulating blood. It is an effective concentration of multiple fundamental growth factors (GF’s) which were stored as α-granules in platelets and plasma proteins
- Degranulation of the prepacked growth factors in platelet occurs upon “activation”
- Activation done by adding Cacl2 or calcium gluconate with PRP in a ratio of 1:9 (CaCl2:PRP)

Figure 9: Before centrifuge

FIGURE 10: After soft spin

FIGURE 11: After hard spin

USES OF PRP IN DERMATOLOGY:

1. Androgenetic alopecia

Androgenetic alopecia (AGA) is a common and psychologically distressing condition affecting both males and females worldwide [70]. Although a variety of management strategies prevail, including minoxidil, finasteride, and hair transplantation, a significant number of patients either remain outside the ambit of these strategies or may not fully respond to treatment. In the last decade, with the advent of PRP, it has been an active area of interest for AGA management. The role of PRP in the management of other alopecias is elusive [71]. Activated PRP stimulates proliferation and differentiation of stem cells in the hair follicle bulge area via multiple molecular mechanisms.

The various mechanisms are:

i. Up regulation of transcriptional activity of βcatenin thereby causing differentiation of stem cells into hair follicle cells
ii. Increased levels of bcl-2 which are anti apoptotic thereby prolonging the survival of cells of dermal papilla
iii. Activation of Akt and ERK signalling pathways leads to increased survival of cells of dermal papilla
iv. Anagen phase of hair is prolonged due to expression of Fibroblast growth factor in the cells of dermal papilla [72]

2. Skin rejuvenation:

The role of PRP in skin rejuvenation by possible improvement in skin elasticity and cosmetic appearance has been proposed to be due to a various mechanisms, including the increased proliferation of cutaneous fibroblasts; increased expression of matrix metalloproteinases (like MMP 1 and 3) which degrade and remove sun damaged extracellular matrix; increased type 1 collagen production and modifying cell cycle regulators. PRP treated human dermal fibroblasts (HDFs) also show a dramatic reduction in phosphorylation of c-Jun N terminal kinase , which further promotes wound healing [73].

3. Chronic ulcers:

The growth factors present in PRP regulate mesenchymal cell recruitment, control proliferation and further promote extra cellular matrix synthesis in chronic wound healing [74]. Topical use of PRP has been reported to significantly improve epithelialization in both acute and chronic ulcers due to several etiologies including stasis, diabetic ulcers, venous, traumatic and even trophic ulcers in leprosy. Thus, PRP seems to be a useful therapy, either alone or in conjunction with other topical therapies, in chronic non-healing wound ulcers due to varied etiologies [75].

4. Acne scars:

PRP has a promising adjunct role in management of acne scars and soft tissue augmentation. The growth factors of PRP act synergistically with growth factors and collagen induction induced by microneedling methods [76].

5. Vitiligo:

PRP has a high concentration of growth factors, which may stimulate melanocyte proliferation and repigmentation in the vitiligo lesions [77]. In a randomized trial, in stable non-segmental vitiligo patients, a combination of PRP with fraction carbon dioxide LASER was more effective in promoting repigmentation than PRP alone or fractional carbon dioxide LASER alone [78].

6. Psoriasis vulgaris:

PRP exerts anti-inflammatory effect which could be mediated by the presence of Hepatocyte Growth Factor (HGF) among other growth factors [79]. Bendinelli et al. explained that PRP exerts inhibitory effect on NFκB pathway through enhanced cellular lκBα expression which consequently retain NF-κB-p65 subunit within cytoplasm and prevent its nucleo-cytoplasmic shuttling [80]. PRP reduces chemotaxis by inhibiting chemokine transactivation and CXCR4-receptor expression, thus possibly controlling local inflammation. In chakravdhanula study, greater percentage of psoriatic patients treated with MTX/PRP accomplished study endpoint of PASI75 at week 16 compared to control group, thereby substantiating curative property of PRP. Hence PRP could enhance efficacy of MTX in directing and accelerating healing process either through additive or synergistic mechanism, thereby decreasing patient's dependence to increasing dose of MTX [81].

7. Other uses:

PRP has found its use in conditions like melasma, as factors like TGF β1 and PDGF have been shown to decrease melanogenesis.

Striae distensae, also known as stretch marks, are cosmetically problematic skin lesions often seen on abdomen, thighs, buttocks, and shoulder regions [82,83].

Pilot studies of combined PRP injections with intradermal radiofrequency device or transdermal PRP with fractional radiofrequency or microdermabrasion were reported good results in female patients with striae distensae [84].

Intralesional PRP injections produced significant improvement in induration and complete reepithelialisation of lipodermatosclerosis [85].

One study reported the significant benefit of three weekly intramatricial PRP injections in refractory nail disorders like nail lichen striatus and idiopathic trachyonychia [86].

Safety of PRP:

- It is a well tolerated procedure. No major side effects are reported
- It is easy to perform. Since it is autologous minimum risk of allergic reactions compared to exogenous compounds and free from concerns over blood borne infections like HIV, Hepatitis B and C [87].

Disadvantages:

Special apparatus is required. It is time consuming and requires special traininig to prepare PRP for use. Local injection site reactions like pain or secondary infection may occur which can be avoided with proper precautions [88].

Aims & Objectives

AIMS AND OBJECTIVES OF THE STUDY

1. To compare the clinical efficacy of intralesional PRP with methotrexate, intralesional methotrexate monotherapy and conventional topical therapy in the treatment of chronic plaque psoriasis.
2. To assess the adverse effects associated with intralesional PRP and intralesional methotrexate.
3. To determine the recurrence rate after treatment.

Materials & Methods

MATERIALS AND METHODS

Study Design:

Randomized controlled trial

Study Centre:

Department of Dermatology, Madras Medical College &

Rajiv Gandhi Government General Hospital, Chennai- 3.

Study period:

One year six months (November 2019 – April 2021)

Study Population:

Patients with localized chronic plaque psoriasis attending OutPatient clinic of Department of Dermatology, Madras Medical College & Rajiv Gandhi Government General Hospital during the study period.

Inclusion criteria

1. Patients of more than 18 years of age attending, the Dermatology OPD during the study period with localized stable plaque psoriasis for 6 months, involving <10% of Body Surface Area and maximum PASI of 10 at the time of screening will be included.
2. Patient who has not undergone any prior systemic or topical treatment.
3. Those who are willing to give consent to participate in the study.

Exclusion criteria:

1. Prior known allergic response to methotrexate.
2. Patients who received any other treatments for their psoriasis before enrollment.
3. Patients with history of renal, liver impairment, allergic skin disorders and blood dyscrasia.
4. Patients with acute febrile illness or signs of any inflammation or infection.
5. Patients with Hepatitis B & Hepatitis C infection
6. Patients with immunosuppression/ HIV Infection
7. Patients with pustular / erythrodermic psoriasis
8. Patients of <18 years of age
9. Pregnant women
10. Patients who are not willing for study

Sample Size:

Sixty six patients (66) attending the OutPatient clinic of Department of Dermatology, Madras Medical College & Rajiv Gandhi Government General Hospital and who satisfied the above criteria were included during the study period.

Methodology:

1. Patients with localized chronic plaque psoriasis were enrolled into the study after obtaining informed consent and randomised into 3 groups by simple random sampling.
2. Meanwhile, detailed clinical history including basic demographic details were taken.
3. General examination, systemic examination and Dermatological examination were done.
4. Investigations - complete hemogram, liver function test, renal function test, lipid profile, urine routine, random blood sugar, VCTC, VDRL & urine pregnancy test were done.
5. 66 patients were randomly divided into three groups as group A, B and C with 22 patients in each group.

- Group A comprised patients who were treated with single shot of 3 ml (each containing 1 x 10^9 platelet/ml) of PRP intralesionally in their first sitting and subsequently followed with intralesional methotrexate of 7.5-25 mg/m^2/week for 4 weeks and it was repeated every month for 4 months or till resolution of lesions (whichever is earlier).
- Group B comprised patients who were treated with intralesional methotrexate of 7.5-25mg/m^2/week alone.
- Group C comprised patients who were treated with conventional topical treatment like emollients and corticosteroids.

After treatment, the patients were followed up for 3 months & digital photographs, PASI score & adverse events (if any) were recorded at weeks 0,4,8,12,16 and 20. Clinical effectiveness, relapse and remission were noted.

STATISTICAL ANALYSIS:

All the data collected were entered into Microsoft excel 2019 to create a master chart. The master chart was then loaded into SPSS version 23 for statistical analysis. Both quantitative and qualitative variables were present in the study. Qualitative variables were expressed using percentages while mean and standard deviation was used to express quantitative variables.

To compare the distribution of qualitative variable between the three arms, Chi square test was used. For comparing mean value of a variable between the three groups, ANOVA (Analysis of variance) test was used. In order to compare the mean of a variable measures at various timeline and also to compare the variation in mean between the groups at all the time line RMANOVA (Repeated Measures Analysis of variance) was used. A P value of less than 0.05 was considered as ‘statistically significant’.

ETHICAL ISSUES:

Institutional ethics committee of Madras Medical College reviewed the study proposal for ethical consideration and approval of the committee was obtained prior to the study.

Observations & Results

OBSERVATION AND RESULTS

Introduction:

66 patients who satisfied the inclusion criteria attending the outpatient clinics of Department of Dermatology at RGGGH, Chennai were included for this study.66 patients were divided into 3 groups equally and randomly.

- Group A: Intralesional PRP in combination with intralesional methotrexate
- Group B: Intralesional methotrexate alone.
- Group C: Topical therapy.

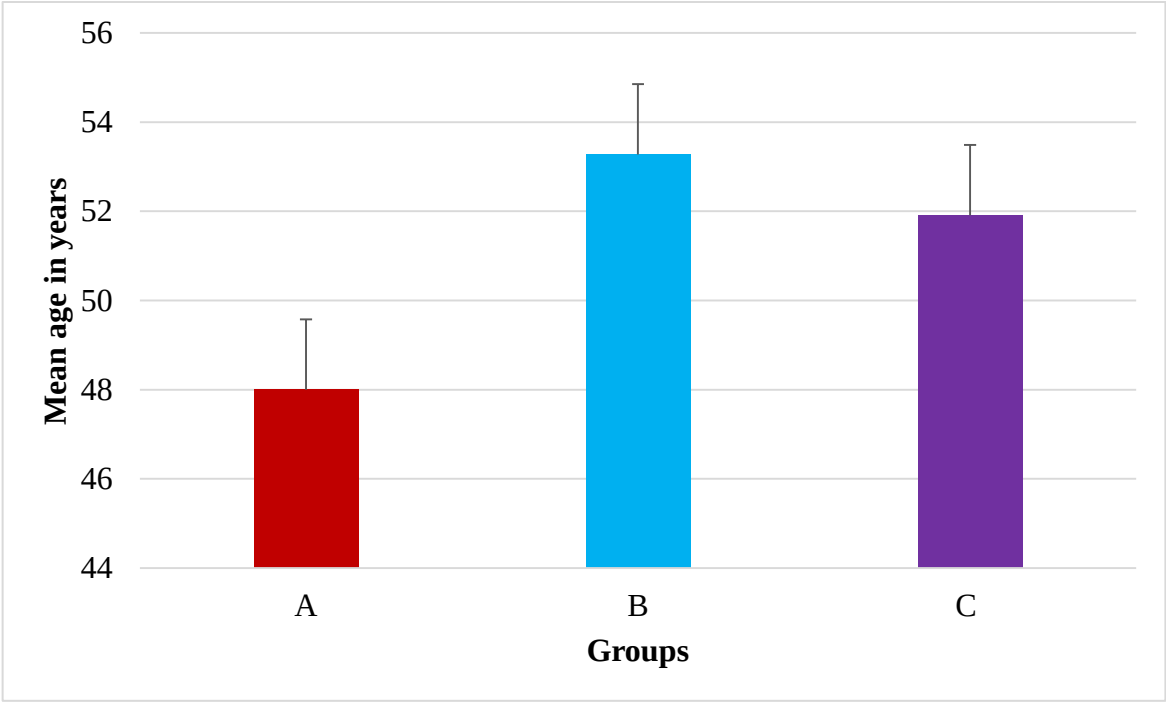
Detailed case history of each patients like age, sex, comorbidities and details regarding psoriasis were noted. General examination, Systemic examination and complete Dermatological examinations were done. All the patients included in the study were subjected to routine investigations such as complete hemogram, renal function test, liver function test, lipid profile, urine routine, urine pregnancy test, VDRL test for syphilis, ELISA for HIV to rule out comorbidities and to initiate appropriate management.

Psoriatic lesions were assessed for degree of Erythema, Scaling, and Induration and PASI score was calculated during each visit. Photographs were taken before and after each treatment.

Table 1: Comparison of mean age between the three arms of the study.

Group	Age (In years)		f	P value*
	Mean	SD		
A	48	10.15	1.26	0.290
B	53.27	14.54		
C	51.91	8.74		

Chart 1: Bar chart comparing the mean age between the groups.

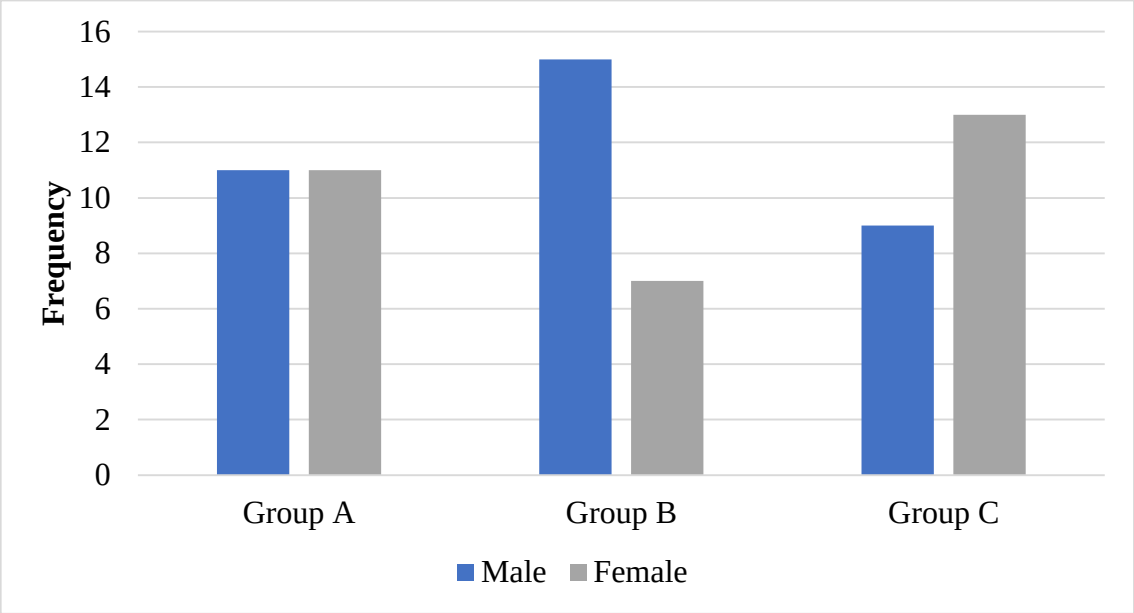


The mean age among the Group A was 48 ± 10.15 years. The mean age among the Group B was 53.27 ± 14.54 years and the mean age among the Group C was 51.91 ± 8.74 years. All the three groups had statistically similar mean age with P value of more than 0.05.

Table 2: Distribution according to the presence of sex between the three arms of the study

Sex	Group A		Group B		Group C		X^2	P value
	N	%	N	%	N	%		
Male	11	50	15	68.2	9	40.9	3.406	0.182
Female	11	50	7	31.8	13	59.1		

Chart 2: Bar chart showing distribution of sex between the three arms of the study.

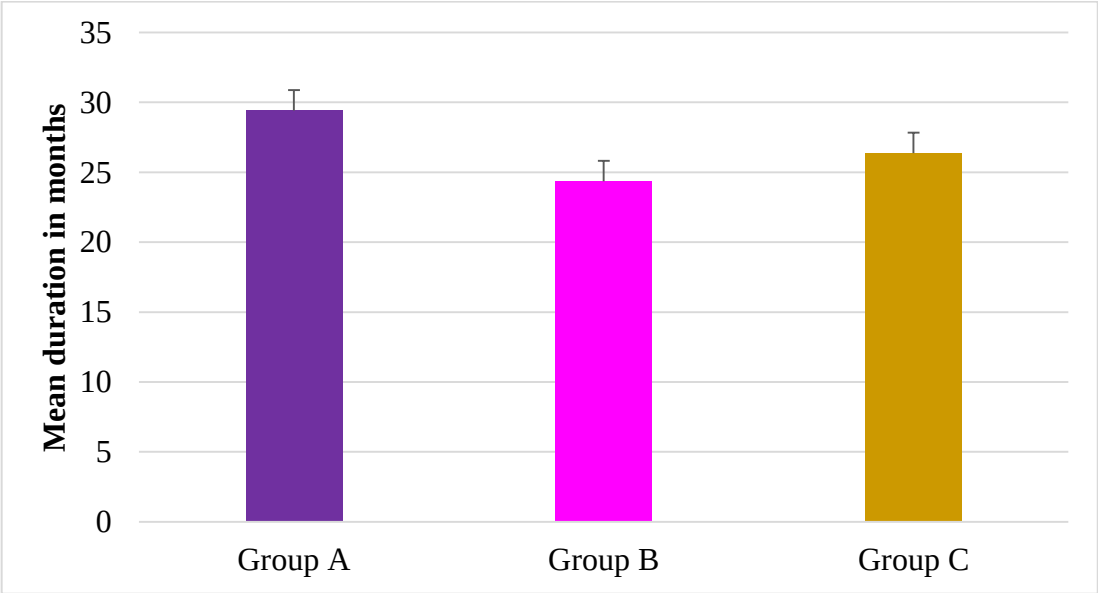


Among the participants in the Group A, 50% were males and among those in the Group B, 68.2% were males. Among the participants in the Group C, 40.9% were males. The distribution of sex was found to be similar in all the three groups with P value of more than 0.05.

Table 3: Comparison of mean duration of disease between the three arms of the study

Group	Duration of disease (In months)		f	P value*
	Mean	SD		
A	29.41	28.28	0.275	0.760
B	24.36	17.30		
C	26.36	21.16		

Chart 3: Bar chart showing comparison of mean duration of disease between the three arms of the study.

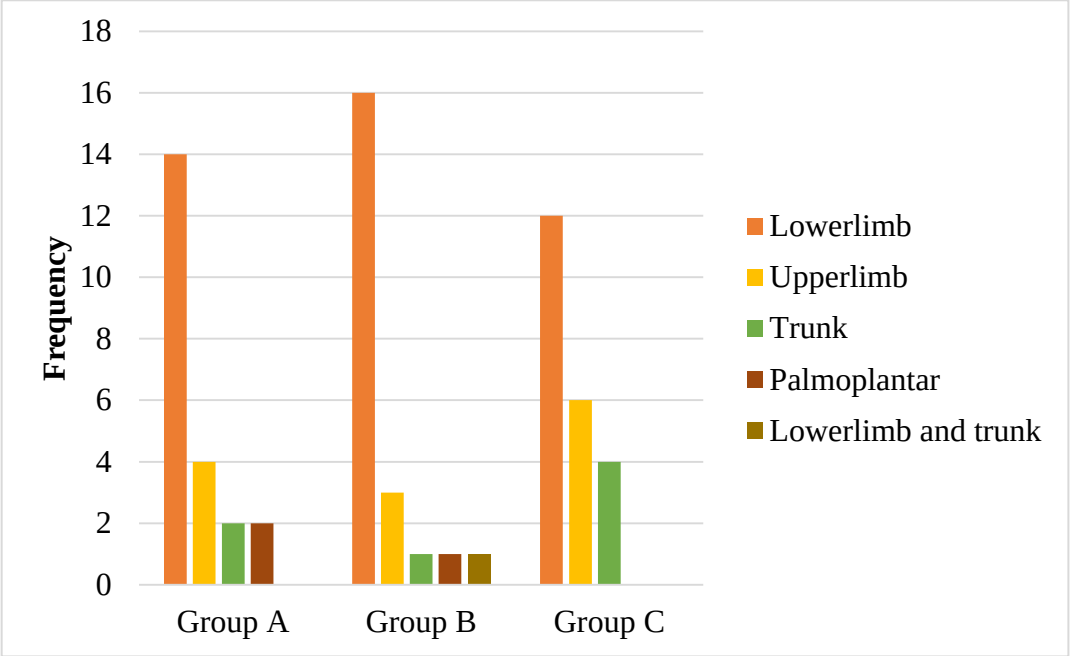


The mean duration of disease among the Group A was 29.41 ± 28.28 months. The mean duration of disease among the Group B was 24.36 ± 17.30 months and the mean duration among the Group C was 26.36 ± 21.16 months. All the three groups had statistically similar mean age with P value of more than 0.05.

Table 4: Distribution according to site of lesion between the three arms of the study

Site of lesion	Group A		Group B		Group C		X^2	P value
	N	%	N	%	N	%		
Lower limb	14	63.3	16	72.7	12	54.5	7.648	0.469
Upper limb	4	18.2	3	13.6	6	27.3		
Trunk	2	9.1	1	4.5	4	18.2		
Palmoplantar	2	9.1	1	4.5	0	0		
Lower limb and Trunk	0	0	1	4.5	0	0		

Chart 4: Bar chart showing distribution of site of lesion between the three arms of the study.

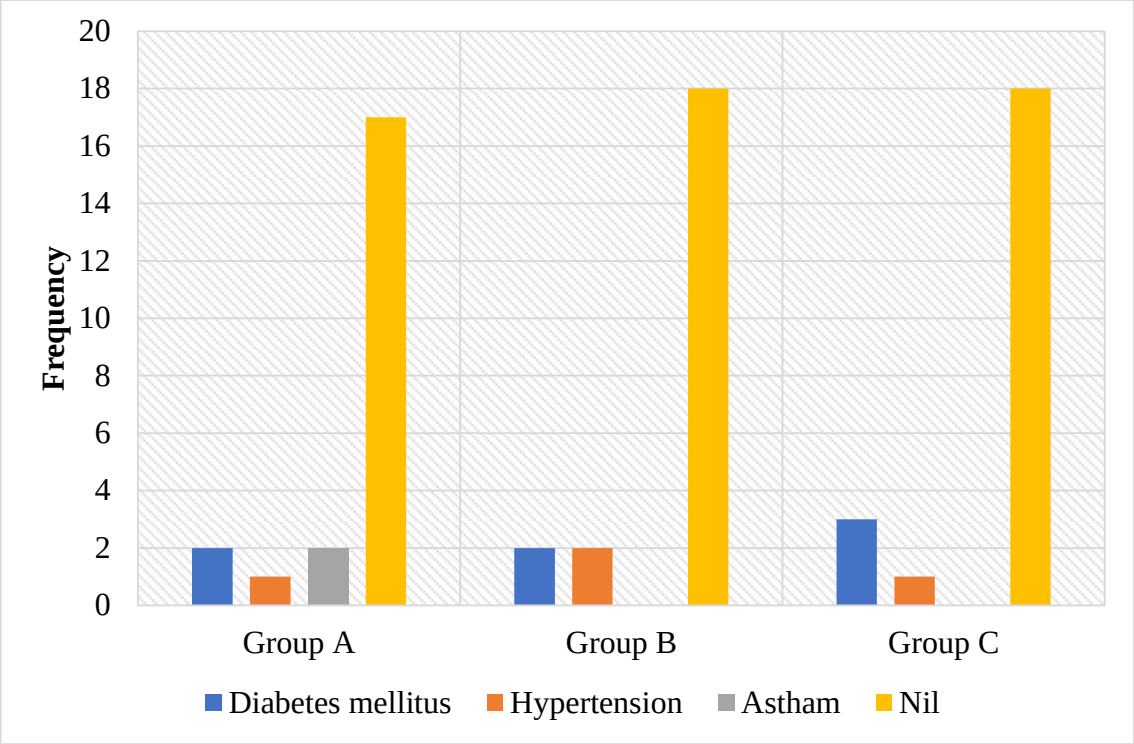


Among the participants in the Group A, 63.3% had lesion in lower limb and 18.2% had lesion in upper limb. Among those in the Group B, 72.7% had lesion in lower limb and 13.6% had it in upper limb. Among those in the Group C, 54.5% had lesion in the lower limb and 27.3% had lesion in the upper limb. The distribution of site of lesion was found to be similar in all the three groups with P value of more than 0.05.

Table 5: Distribution according to the presence of comorbidities between the three arms of the study.

Comorbidities	Group A		Group B		Group C		X^2	P value
	N	%	N	%	N	%		
Diabetes mellitus	2	9.1	2	9.1	3	13.6	4.823	0.567
Hypertension	1	4.5	2	9.1	1	4.5		
Asthma	2	9.1	0	0	0	0		
Nil	17	77.3	18	81.8	18	81.8		

Chart 5: Bar chart showing distribution of comorbidities between the three arms of the study.

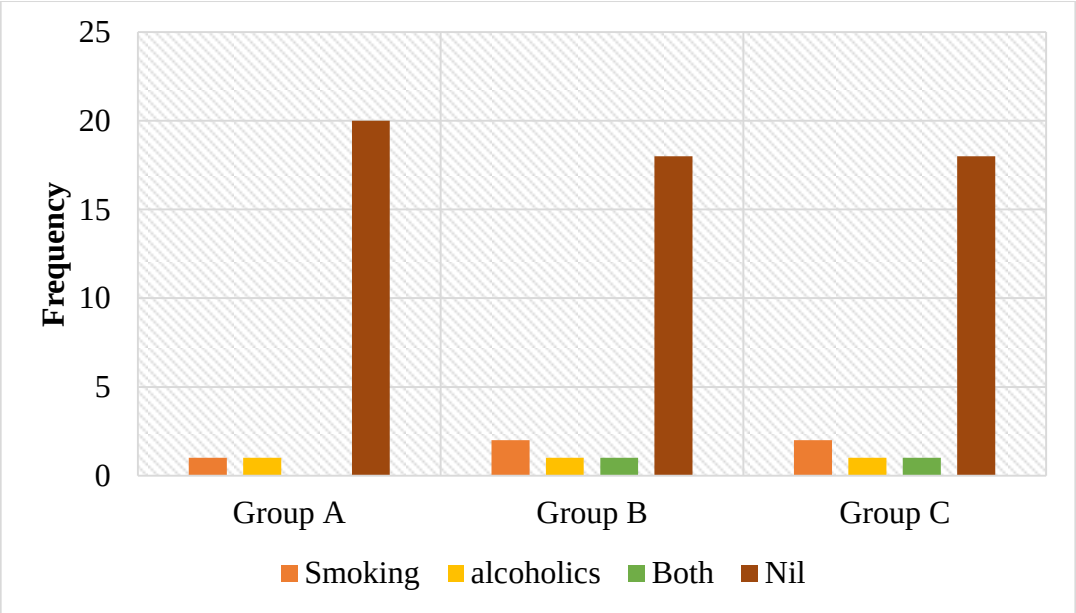


Among the participants in the Group A, 9.1% had diabetes mellitus, 9.1% had asthma and 4.5% had hypertension. Among the participants in the Group B, 9.1% had diabetes and hypertension, respectively. Among the participants in the Group C, 13.6% had diabetes mellitus and 4.5% had hypertension. The distribution of comorbidities was found to be statistically similar between the groups with P value of more than 0.05.

Table 6: Distribution according to the presence of substance abuse between the three arms of the study.

Substance abuse	Group A		Group B		Group C		X^2	P value
	N	%	N	%	N	%		
Smoking	1	4.5	2	9.1	2	9.1	1.543	0.957
Alcoholism	1	4.5	1	4.5	1	4.5		
Both	0	0	1	4.5	1	4.5		
Nil	20	90.9	18	81.8	18	81.8		

Chart 6: Bar chart showing distribution of substance abuse between the three arms of the study.



Among the participants in the Group A, 4.5% were smokers and alcoholics, respectively. Among the participants in the Group B, 9.1% were smokers, 4.5% were alcoholics and 4.5% were both smokers and alcoholics. Among those in the Group C, 9.1% were smokers, 4.5% were alcoholics and 4.5% were both smokers

and alcoholics. The distribution of substance abusers was found to be statistically similar between the groups with P value of more than 0.05.

Complete blood count, liver function test and renal function tests were found to be normal in all the study participants who participated in the study irrespective of the study arms that they belonged to.

Table 7: Change in mean PASI over the time line in all the three arms of the study.

Timeline	Group A		Group B		Group C	
	Mean	SD	Mean	SD	Mean	SD
Pre treatment	3.41	1.14	3.35	0.93	3.46	1.05
After 1 month	3.29	1.10	3.30	0.91	3.37	1.15
After 2 months	2.81	1.09	3.14	1.01	3.15	1.08
After 3 months	2.41	0.97	2.97	1.01	2.83	1.01

Chart 7: Line diagram showing change in mean PASI over the timeline.

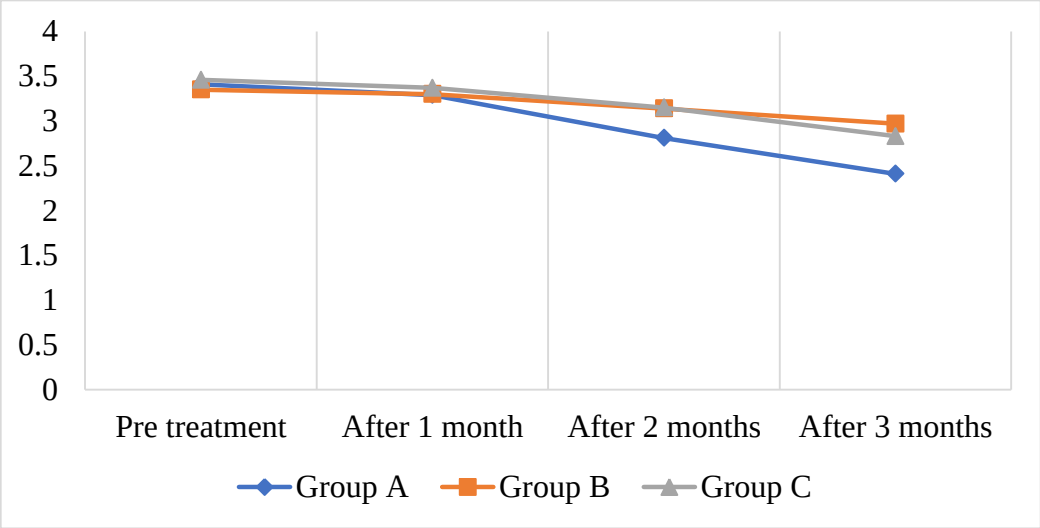


Table 8: Repeated measures ANOVA for finding the significance of change within and between the groups.

Condition	F value	P value
Within each group	3.554	0.013
Between the groups	0.348	0.707

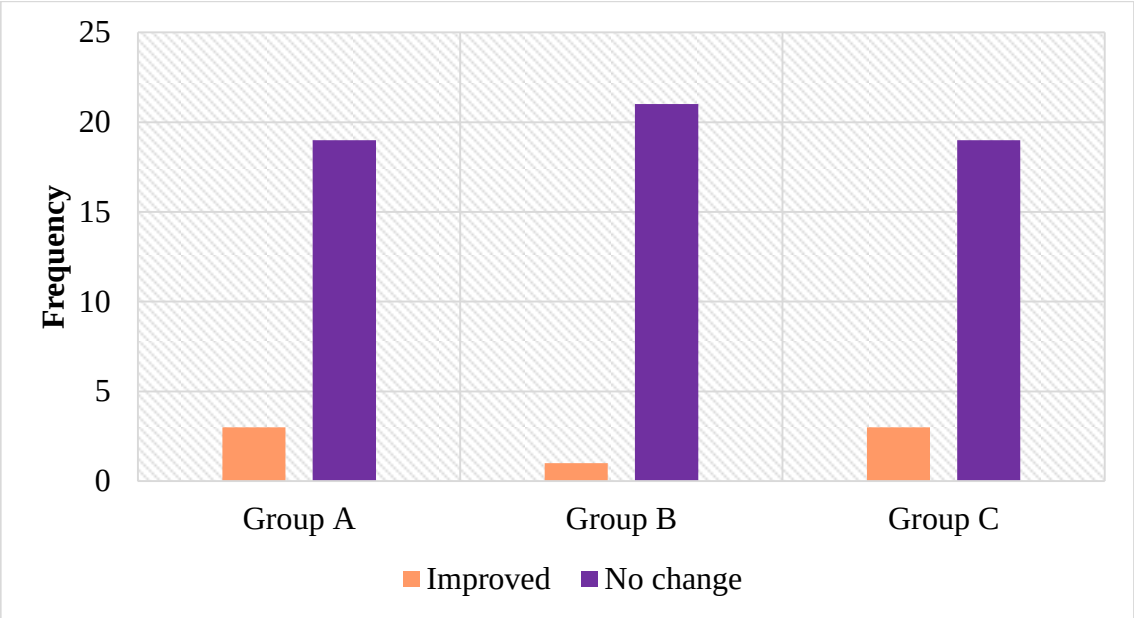
The mean PASI at the pre-treatment level in Group A,B and C were 3.41 ± 1.14, 3.35 ± 0.93 and 3.46 ± 1.05, respectively. In all the three groups, there was decrease in the magnitude of the mean PASI during each follow up visits at the 1^{st},2^{nd} and 3^{rd} months. The mean PASI at the end of third month in Group A was 2.41 ± 0.97, that of Group B was 2.97 ± 1.01 and that of Group C was 2.83 ± 1.01. The final PASI score was lesser in Group A, followed by Group C and Group B had the highest.

Within all the three groups there was statistically significant reduction in the PASI score (P value < 0.05). There was no statistically significant difference in reduction when the three groups were compared between them.

Table 9: Distribution of results between the groups at the end of first month.

Results at the end of 1st month	Group A		Group B		Group C		X^2	P value
	N	%	N	%	N	%		
Improved	3	13.6	1	4.5	3	13.6	1.278	0.528
No change	19	86.4	21	95.5	19	86.4		

Chart 8: Bar chart showing distribution of results between the groups at the end of first month.

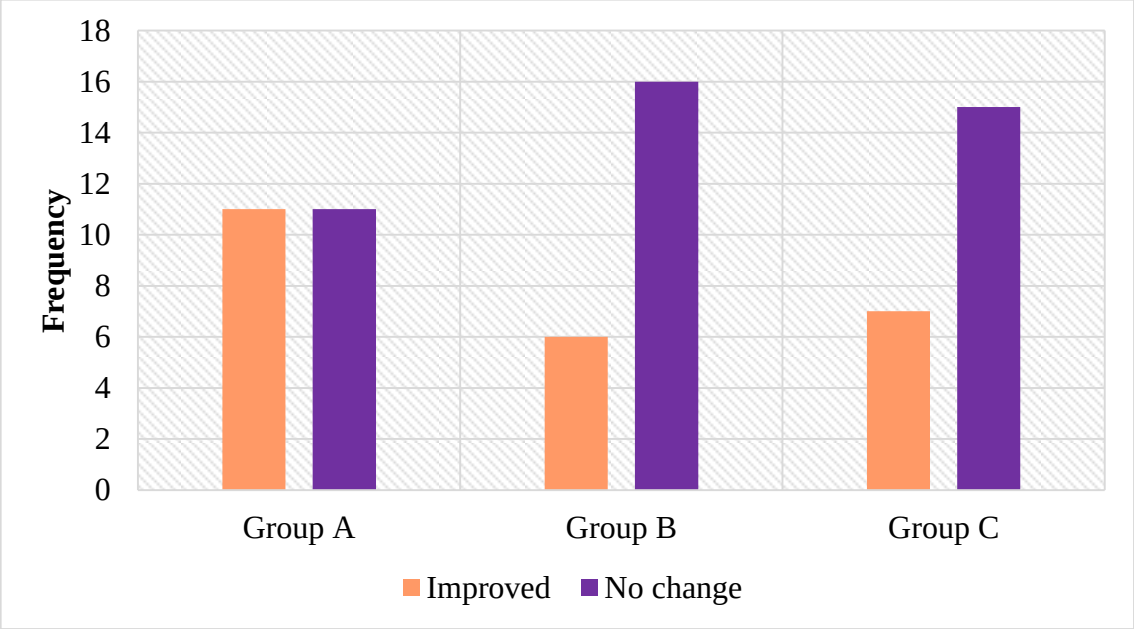


Among the participants in the Group A, 13.6% had shown improvement after 1st month. Among the participants in the Group B, 4.5% had shown improvement and among those in the Group C, 13.6% had shown improvement at the end of 1st month. The distribution of results in all the three groups was statistically similar with P value of more than 0.05.

Table 10: Distribution of results between the groups at the end of second month.

Results at the end of 2nd month	GroupA		Group B		Group C		X^2	P value
	N	%	N	%	N	%		
Improved	11	50	6	27.3	7	31.8	2.75	0.253
No change	11	50	16	72.7	15	68.2		

Chart 9: Bar chart showing distribution of results between the groups at the end of second month.

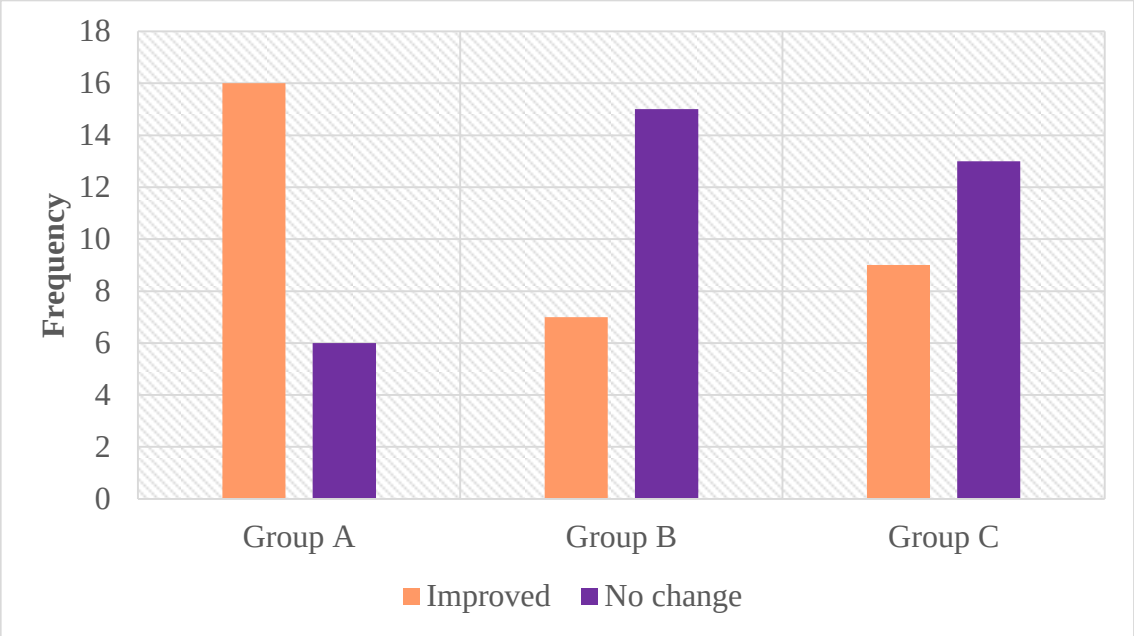


Among the participants in the Group A, 50% had shown improvement after 2nd month. Among the participants in the Group B, 27.3% had shown improvement and among those in the Group C, 31.8% had shown improvement at the end of 2nd month. The distribution of results in all the three groups were statistically similar with P value of more than 0.05.

Table 11: Distribution of results between the groups at the end of third month.

Results at the end of 3rd month	Group A		Group B		Group C		X^2	P value
	N	%	N	%	N	%		
Improved	16	72.7	7	31.8	9	40.9	8.129	0.017
No change	6	27.3	15	68.2	13	59.1		

Chart 10: Bar chart showing distribution of results between the groups at the end of third month.

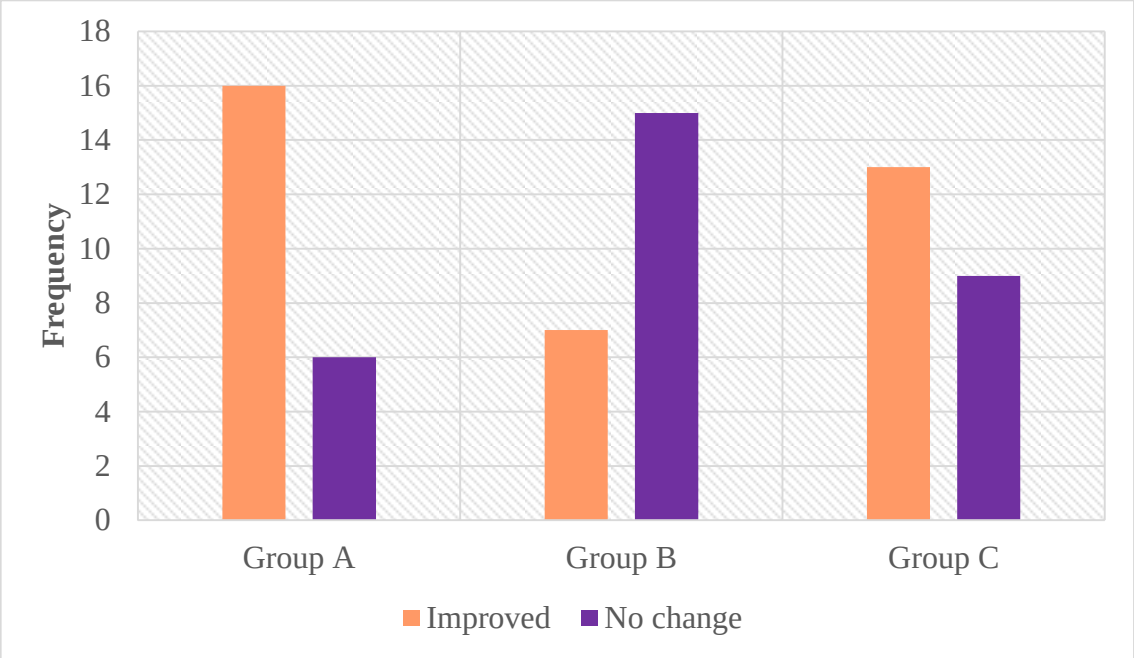


Among the participants in the Group A, 72.7% had shown improvement after 3rd month. Among the participants in the Group B, 31.8% had shown improvement and among those in the Group C, 40.9%% had shown improvement at the end of 3rd month. The proportion of participants showing improvement was more in the PRP group than the rest of the group. The above difference was found to be statistically significant with P value of less than 0.05.

Table 12: Distribution of overall results between the groups.

Overall results	Group A		Group B		Group C		X^2	P value
	N	%	N	%	N	%		
Improved	16	72.7	7	31.8	13	59.1	7.700	0.021
No change	6	27.3	15	68.2	9	40.9		

Chart 11: Bar chart showing distribution of overall results between the three arms of the trial.



Among the participants in the Group A, 72.7% had shown improvement. Among the participants in the Group B, 31.8% had shown improvement and among those in the Group C, 59.1%% had shown improvement. The proportion of participants showing improvement was more in the Group A than the rest of the group. The above difference was found to be statistically significant with P value of less than 0.05.

Table 13: Distribution of adverse events between the three arms of the trial.

Adverse events	Group A		Group B		Group C		X^2	P value
	N	%	N	%	N	%		
Pain	7	31.8	3	13.6	0	0	13.47	0.036
Irritation	1	4.5	1	4.5	0	0		
Depigmentation	0	0	0	0	2	9.1		
Nil	14	63.6	18	81.8	20	90.9		

Among the participants in the Group A, 31.8% reported pain and 4.5% reported irritation. Among the participants in the Group B, 13.6% reported pain and 4.5% reported irritation. Among the participants in the Group C, 9.1% had reported depigmentation. The proportion of participants with adverse events especially pain was more in the Group A participants treated group than the rest of the groups. The above difference was found to be statistically significant with P value of less than 0.05.

Table 14: Distribution according to recurrence between the groups.

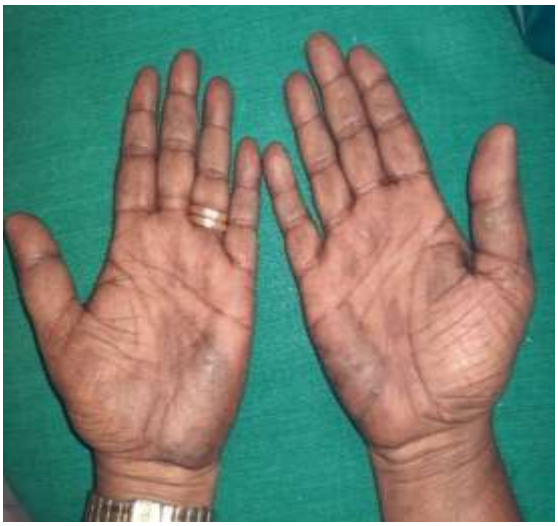
Recurrence	Group A		Group B		Group C		X^2	P value
	N	%	N	%	N	%		
Yes	2	9.1	3	13.6	5	22.7	1.68	0.793
No	15	68.2	14	63.6	13	59.1		
Lost to follow up	5	22.7	5	22.7	4	18.2		

Among the participants in the Group A, 9.1% had recurrence. Among those treated with intralesional methotrexate alone, 13.6% had recurrence and in the topical therapy group, 22.7% had recurrence. All the groups were found to be statistically similar as far as ‘P value’ is concerned, wherein they all had a p value of more than 0.05.

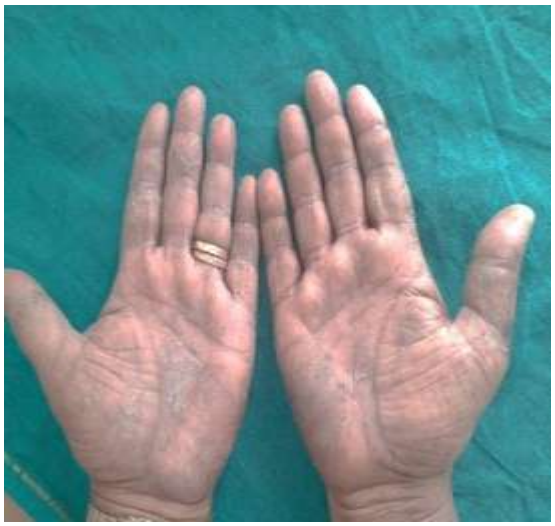
Clinical Images

CLINICAL IMAGES

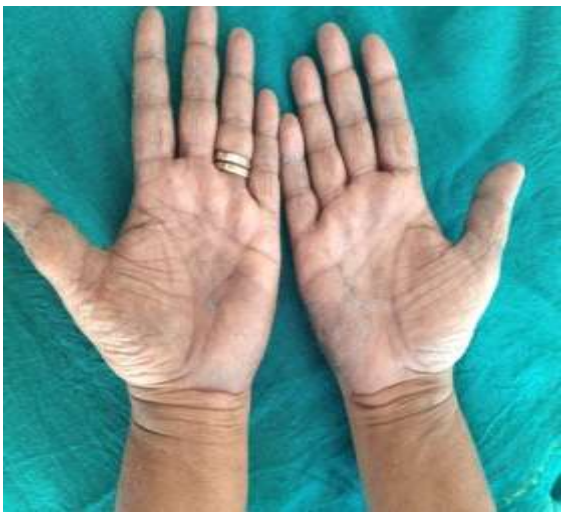
GROUP A: INTRALESIONAL PRP IN COMBINATION WITH INTRALESIONAL METHOTREXATE



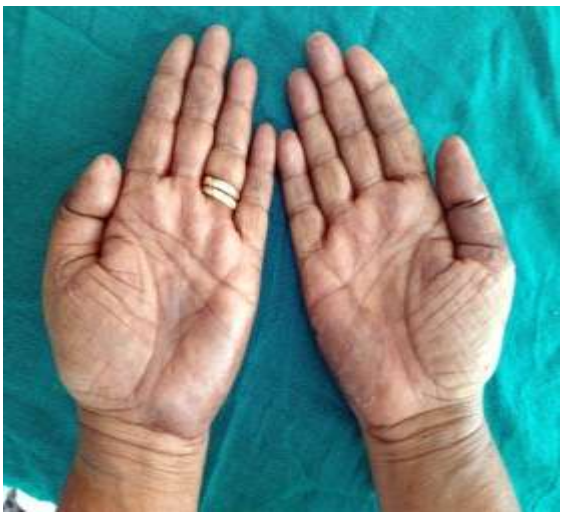
Before treatment



End of first month follow up

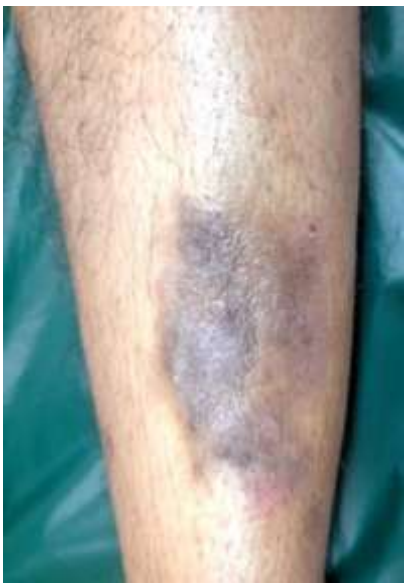


End of second month follow up

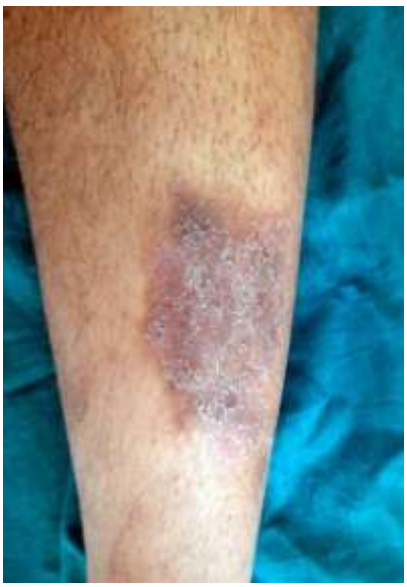


End of third month follow up

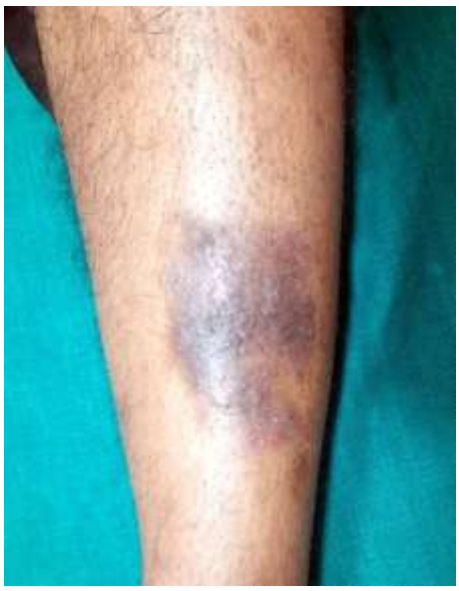
GROUP B: INTRALESIONAL METHOTREXATE MONOTHERAPY



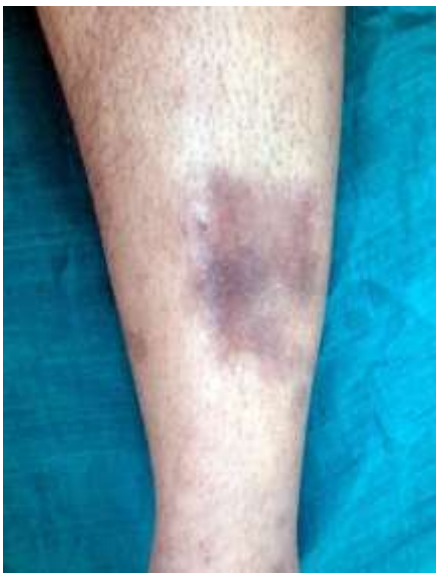
Before treatment



End of first month follow up

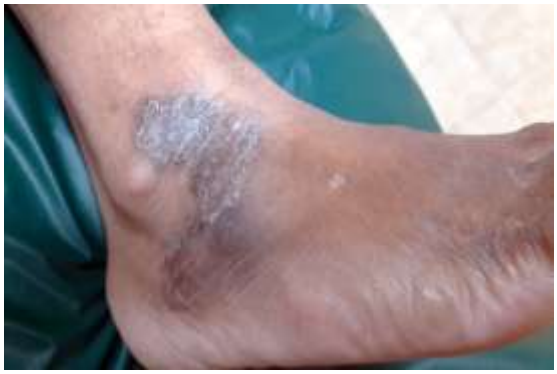


End of second month follow up

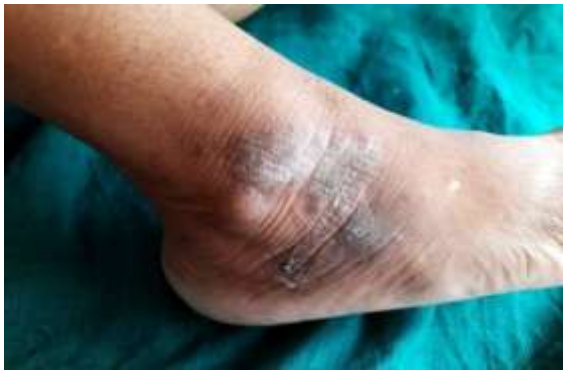


End of third month follow up

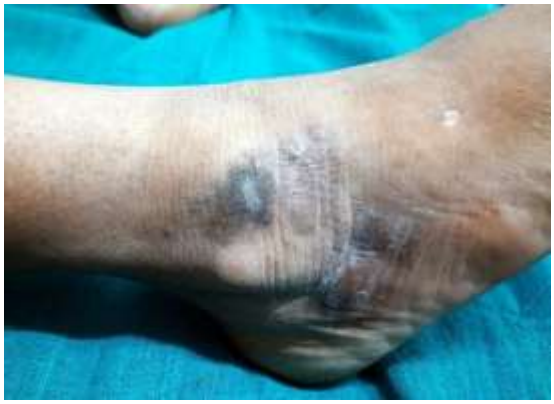
GROUP C: TOPICAL THERAPY



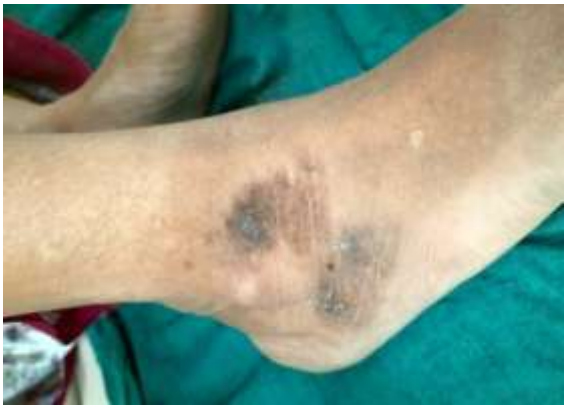
Before treatment



End of first month follow up



End of second month follow up



End of third month follow up

Discussion

DISCUSSION

Recognition of psoriasis, as well as it's associated medical and psychiatric complications can facilitate timely diagnosis and appropriate management. This study was conducted in a tertiary care hospital to compare the efficacy of PRP in combination with methotrexate, methotrexate monotherapy and conventional topical therapy in the treatment of chronic plaque psoriasis. In this study totally 66 patients with chronic plaque psoriasis were included. The patients were randomly distributed into three groups namely Group A, Group B and Group C with 22 patients in each group. All the patients in Group A had undergone treatment with single shot of PRP intralesionally in their first sitting and subsequently followed with intralesional methotrexate for 4 weeks and it was repeated every month for 4 months or till resolution of lesions (whichever is earlier). All the patients in group B were treated with intralesional methotrexate and group C topical corticosteroids. The patients in this study were most commonly in the age group of 51- 60 years which includes 23(34.8%) patients. The second most common age group is 41-50 years with 20(30%) patients. The mean age in this study was 50.6 years.

While the mean age of psoriasis patients in Chakravdanula et al. was 40 years [80] and in Winfried study [35] the mean age was 52 years. The below tabular column shows the mean age of psoriasis patients in various age groups.

Table 15: Comparison of mean age in various studies:

STUDY NAME	MEAN AGE
This study	50.6 years
Chakravdhanula et al	40 years
Winfried study	52 years

In this study, there were 11males and 11 females in group A. In group B, there were 15 male and 7 female and 9 male and 13 female in group C. The distribution of sexes among all the three groups were statistically similar. Majority of patients in this study had disease duration of 2.3 years. The mean duration of disease among the PRP group was 29.41 ± 28.28 months. The mean duration of disease among the MTX group was 24.36 ± 17.30 months and the mean duration among the topical group was 26.36 ± 21.16 months. All the three groups had statistically similar mean age with P value of more than 0.05. But in the study conducted by Chakravdhanula et al[80] mean duration of disease was 3.7 years.

In this study, among the participants in all the three groups, more of lower limb involvement was noted followed by upper limb involvement and 13.6% had only palmoplantar involvement. In the study conducted by Winfried [35] upper limb involvement is more common. The distribution of site of lesion was found to be similar in all the three groups with P value of more than 0.05.

In our study 7(10.6%) of the subjects had diabetes, 4 (6%) of the subjects with hypertension and 2 (3%) of the subjects were asthmatics. 5 (7%) participants were smokers, 3 (4.5%) participants were alcoholics and 2 (3%) of them were both smokers and alcoholics.

The mean PASI score at the pre-treatment level in Group A was 3.41±1.14, in Group B was 3.35±0.93 and in Group C was 3.46±1.05. In a study by Winfried the average size of lesion of study population was 8.2 cm2 [35]. Whereas in a study by Chakravdhanula et al the PASI score was ranging from 9-35 [80].

Analysis of treatment response after first month of treatment:

After completion of three months of treatment in both treatment groups the response to treatment was analysed by taking photographs and comparing with pre-treatment photographs, PASI score & adverse events (if any) at the end of 1,2 and 3 months of treatment. Clinical effectiveness, relapse and remission were noted. Out of 22 participants in the PRP group, 3 (13.6%) had shown improvement and 19 (86.4%) maintained their pre-treatment stage after 1st month. Among the 22 participants in the MTX group, only one (4.5%) had shown improvement and among those in the topical group, 3 (13.6%) had shown improvement at the end of 1st month. By applying chi-square test there was no significant improvement in all the 3 groups and the distribution of results in all the three groups were statistically similar after 1 month of treatment with a ‘p’ value of more than 0.05. So at the end of first month of treatment none of the group showed significant improvement. It implies that one month of treatment was not

adequate in all the three groups. So patients should not be evaluated for the efficacy of treatment response for any modality at the end of first month and needs longer periods of treatment. This emphasizes the need for counselling the patients pertaining to their expectations and the realistic response. This aids to improve patient compliance and prevents the unrealistic expectations from the patient's outlook and thus prevents them from going into depression.

Analysis of treatment response after second month of treatment:

The patients were analysed after completion of six months of treatment in all the three groups for treatment response by taking photograph again at the end of second month and compared with the photographs taken before starting treatment and after one month and they were compared. Among the participants in the group A, 11 (50%) had shown improvement after second month. Among the participants in the group B, (6) 27.3% had shown improvement and among those in the topical therapy group, 7 (31.8%) had shown improvement at the end of 2nd month. The distribution of results in all the three groups were statistically similar with P value of more than 0.05. In all the three groups, the total number of patients showing improvement has become more at the end of second month of management. Among the three groups, Group A participants who were treated with PRP in combination with methotrexate had shown higher proportion of improvement.

Analysis of treatment response after third month of treatment:

The patients were analysed after completion of three months of treatment in all the three groups. Among the participants in the group A, 16 (72.7%) had shown improvement after 3rd month. Out of total 22 participants who were treated with intralesional methotrexate alone, 7 (31.8%) had shown improvement and among those in the topical management group, 9 (40.9%) had shown improvement at the end of 3rd month. The proportion of participants showing improvement was more in the PRP group than the rest of the group. The above difference was found to be statistically significant with P value of less than 0.05.

Overall analysis of treatment response at the end of the follow up in the three groups of the trial:

In Group A 16(72.7%) patients improved and 6 (27.3%) had no change in their stage, they neither improved nor had progression of lesions. In Group B, 15(68.2%) patients had no change in their stage of disease when compared before treatment and 7(31.8%) patients improved and no patients progressed. In Group C, 13 patients had shown improvement.

The improvement percentage is 72.7% in Group A whereas in Group B it is 68.2% and in Group C it is 31.8%. The proportion of participants showing improvement was more in the PRP group than the rest of the group. There was statistically significant difference between the three groups with a ‘p’ value of less than 0.05 by applying Chi-square test with Group A (PRP in combination with

methotrexate) showing better response than Group B (methotrexate monotherapy) and Group C (topical therapy).

Group A patients were subjected to intralesional injection with PRP in their first sitting and subsequently followed with intralesional methotrexate weekly for 4 weeks and it was repeated every month for 4 months or till resolution of lesions (whichever is earlier). Group B patients were subjected to intralesional methotrexate therapy alone. This shows that intralesional methotrexate as a single modality is not effective than combining it with other modalities such as PRP. Chakravdhanula et al. have reported similar better outcomes in the PRP with methotrexate group vs. the methotrexate group alone. At week 16, all patients in their combinational therapy group achieved PASI 50 and 12.5% achieved PASI 90. None of the patient in the monotherapy group attained PASI 50, however they showed some improvement in the range of 35-40% comparing to the baseline PASI [80]. In Winfried study, 80% of the study population achieved complete remission and the remaining 20% showed improvement in the range of 70-80% comparing to the baseline PASI [35].

This study shows that minimal treatment response of psoriasis vulgaris to a particular modality of treatment in a specific patient can be made out at the end of two months of treatment at least, and in some patients still it needs some more time to determine whether a particular patient is responding to specific modality of treatment or not. So the patients have to be counselled regarding the minimal

duration to appreciate treatment response, varying response with different modalities of management and inter individual variability of responses.

The common side effects observed in this study in Group A, are pain at the time of injection which is seen in 31.8% of patients, followed by irritation during and after injection which is seen in 4.5% of patients. In Group B patients similar complaints of pain and irritation were reported during and after treatment. Among the participants in the Group C, 9.1% had reported depigmentation.

At the end of the follow up of one month after the treatment completion, 9.1% had recurrence among the participants of Group A. Among those treated with methotrexate alone, 13.6% had recurrence and in the Group C, 22.7% had recurrence. All the groups were found to be similar statistically with P value of more than 0.05.

Conclusion

CONCLUSION

- The mean duration of the disease was 2.3 years (27.6 months).When the patients present in their early stage of the disease, the treatment response will be better.
- In our study, there was significant improvement noted both with PRP in combination with methotrexate and topical corticosteroids therapy with emollients.
- But the magnitude of improvement was higher in patients treated with PRP in combination with intralesional methotrexate.
- There is statistically significant improvement in Group A when compared to Group B at the end of third month of treatment.
- So intralesional methotrexate monotherapy as a single modality of treatment in patients with psoriasis is not as effective when compared to PRP with intralesional monotherapy.
- Similarly topical corticosteroids therapy group showed significant improvement at third month than intralesional methotrexate monotherapy.
- The occurrence of adverse effects profile were also statistically similar between PRP with intralesional methotrexate group and intralesional methotrexate monotherapy group.

- The patients have to be counselled regarding the modality of treatment to be used, when to expect response, about the natural course of disease, adherence to treatment before starting treatment.
- The recurrence rates are minimal in all the three groups of treatment.

Limitation

LIMITATIONS

In our study, there were certain limitations. The sample size was small in our study. Although the drugs were given intralesionally, it can act systemically and may have effect on the disease process. So the improvement cannot be attributed to a single drug. The follow up was done only for a limited time.

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Annexures

ABBREVIATIONS

ACE	-	ANGIOTENSIN CONVERTING ENZYME
AGA	-	ANDROGENETIC ALOPECIA
AICAR	-	AMINO IMIDAZOLE-4-CARBOX AMIDO RIBO NUCLEOTIDE
CARD	-	CASPASE ACTIVATION RECRUITING DOMAIN
CD	-	CLUSTER DIFFERENTIATION
CLA	-	CUTANEOUS LYMPHOCYTE ANTIGEN
CXCR	-	C-X-C CHEMOKINE RECEPTOR
DHFR	-	DIHIDRO FOLATE REDUCTASE
EGFR	-	EPIDERMAL GROWTH FACTOR RECEPTOR
ERK	-	EXTRACELLULAR SIGNAL REGULATED KINASE
GF's	-	GROWTH FACTORS
GIT	-	GASTRO INTESTINAL TRACT
GM-CSF	-	GRANULOCYTE MONOCYTE COLONY STIMULATING FACTOR
GR	-	GLUCOCORTICOID RECEPTOR
GRE	-	GLUCOCORTICOID RESPONSE ELEMENTS
HDF	-	HUMAN DERMAL FIBROBALST
HGF	-	HEPATOCYTE GROWTH FACTOR
HLA	-	HUMAN LEUKOCYTE ANTIGEN
IBD	-	INFLAMMATORY BOWEL DISEASE
iNOS	-	INDUCIBLE NITRIC OXIDE SYNTHASE
IL	-	INTERLEUKIN
KGF	-	KERATINOCYTE GROWTH FACTOR
L-PRP	-	LEUKOCYTE AND PLATELET RICH PLASMA
L-PRF	-	LEUKOCYTE AND PLATELET RICH FIBRIN
MAPK	-	MITOGEN ACTIVATED PROTEIN KINASE
MHC	-	MAJOR HISTOCOMPATABILITY COMPLEX
MMP	-	MATRIX METALLO PROTEINASE
MTX	-	METHOTREXATE
MRP	-	MULTIDRUG RESISTANT PROTEIN FAMILY

NFκB	-	NUCLEAR FACTOR LIGHT CHAIN ENHANCER OF ACTVATED B CELL
NSAID	-	NON STEROIDAL ANTI INFLAMMATORY DRUG
OD	-	ONCE DAILY
OPD	-	OUT PATIENT DEPARTMENT
PASI	-	PSORIASIS AREA SEVERITY INDEX
PUVA	-	PSORALEN ULTRA VIOLET A
PDGF	-	PLATELET DERIVED GROWTH FACTOR
PPP	-	PLATELET POOR PLASMA
PRP	-	PLATELET RICH PLASMA
P-PRP	-	PURE PLATELET RICH PLASMA
P-PRF	-	PURE PLATELET RICH FIBRIN
PUVA	-	PSORALEN ULTRA VIOLET A
RANTES	-	REGULATED ON ACTIVATION, NORMAL T EXPRESSED AND SECRETED
RFC	-	REDUCED FOLATE CARRIER
RNA	-	RIBONUCLEIC ACID
TCS	-	TOPICAL CORTICOSTEROIDS
TEN	-	TOXIC EPIDERMAL NECROLYSIS
TGF	-	TRANSFORMATION GROWTH FACTOR
VCTC	-	VOLUNTARY COUNSELLING AND TESTING CENTRE
VDRL	-	VENEREAL DISEASE RESEARCH LABORATORY
VEGF	-	VASCULAR ENDOTHELIAL GROWTH FACTOR

KEY TO MASTER CHART

MTX	-	METHOTREXATE
PRP	-	PLATEELT RICH PLASMA
DM	-	DIABETES MELLITUS
HT	-	HYPERTENSION
PASI	-	PSORIASIS AREA SEVERITY INDEX
UL	-	UPPERLIMB
LL	-	LOWERLIMB
CBC	-	COMPLETE BLOOD COUNT
RFT	-	RENAL FUNCTION TEST
LFT		LIVER FUNCTION TEST

PROFORMA

Serial No.

Name : Age: Sex:

Address:

Educational Qualification:

Occupation: Income:

PRESENTING COMPLAINTS:

H/O Raised lesion

Onset

Sites

Duration

Remission & exacerbation

H/O scaling

H/O itching over the lesion

H/O pus filled lesion

H/O redness & scaling throughout the course of illness

H/O Fever

MARITAL HISTORY:

Marital Status:

Married since:

Pregnancy status:

FAMILY HISTORY:

H/O similar complaints in family members.

TREATMENT HISTORY:

Topical applications

Phototherapy

H/O taking any drug intake

PAST HISTORY:

H/O Allergic response to vaccines

H/O Atopy/Allergic skin disorders /HIV

H/O Diabetes Mellitus/Systemic Hypertension /Bronchial asthma/Pulmonary Tuberculosis/Epilepsy/Jaundice

H/O Surgery/Blood transfusion

PERSONAL HISTORY:

Smoking- Alcoholism- Drug abuse/Drug allergy-

EXAMINATION

1. GENERAL EXAMINATION:
   General Condition:
   Pallor: Icterus: Cyanosis: Clubbing:
   Lymphadenopathy: Pedal edema:

2. SYSTEMIC EXAMINATION:
   Cardiovascular System:
   Respiratory System:
   Per Abdomen Examination:
   Central Nervous System Examination:
3. LOCAL EXAMINATION: EXAMINATION OF LESION:
   Site

   Number

   Size

   Shape

   Scales

   Auspitz sign

   Koebners phenomenon

   Presence of pustules- Erythema-

SCALP : ORAL MUCOSA:

GENITALIA: NAILS:

PALMS & SOLES:

BLOOD INVESTIGATIONS:

Complete blood count

Renal function test

Liver function test

Fasting lipid profile
VDRL, VCTC

4. FOLLOW UP new lesion(if any) PASI Score Side effects
   0 week
   4 week
   8 week
   12 week
   16 week
   20 week

INFORMATION SHEET

We are conducting a study on**"A COMPARATIVE STUDY ON CLINICAL EFFICACY OF PLATELET RICH PLASMA IN COMBINATION WITH METHOTREXATE VERSUS METHOTREXATE MONOTHERAPY VERSUS CONVENTIONAL TOPICAL THERAPY IN CHRONIC PLAQUE PSORIASIS ''** in patients attending Department Of Dermatology at Madras Medical College & Rajiv Gandhi Government General Hospital, Chennai and your co-operation may be valuable to us.

- The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.
- Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled.
- The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

After proper informed consent, detailed clinical history (presenting complaints, past history, personal history any treatment taken) will be elicited. The subjects will undergo complete general, physical and dermatological examination. Then after proper consent from the patient, treatment will be started with either single shot of 3 ml (each containing 1 x 10^9 platelet/ml) of PRP intralesionally in their first sitting & subsequently followed with intralesional methotrexate 7.5-25mg/m^2/week for 4 weeks or intralesional methotrexate or conventional topical therapy and will be repeated every month for 4 months or till resolution of lesions (whichever is earlier) .Treatment response will be assessed every 4 weeks for up to 3 months.

Signature of Investigator Signature of Participant

Date

PATIENT CONSENT FORM

Title of the study: "A COMPARATIVE STUDY ON CLINICAL EFFICACY OF PLATELET RICH PLASMA IN COMBINATION WITH METHOTREXATE VERSUS METHOTREXATE MONOTHERAPY VERSUS CONVENTIONAL TOPICAL THERAPY IN CHRONIC PLAQUE PSORIASIS '' at the Department Of Dermatology at Madras Medical College & Rajiv Gandhi Government General Hospital, Chennai

Name of the participant:

Name of the principal investigator: Dr. B.Yuva priya

Name of the Institution: Department Of Dermatology, Madras Medical College

& Rajiv Gandhi Government General Hospital, Chennai – 3.

Documentation of the informed consent:

I ---------- have read the information in this form (or it has been read to me). 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 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 to me

3. I have been explained about the nature of the 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 him/her immediately if I suffer unusual symptoms

6. I have not participated in any research study at any time

7. I am unaware 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 investigator to release the information obtained from me as a result of participation in this study to the sponsors, 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 the study, I should contact at one of the addresses listed above. By signing this consent form I attest that the information given in this document has been clearly explained to me and apparently understood by me, I will be given a copy of this consent document.

Signature of Participant

For adult participants:

Name and signature/ thumb impression of the participant (or legal representative if participant 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

ஆய்வு தகவல் தாள்

ஆராய்ச்சியின் தலைப்பு :

மெத்தோட்ரெக்ஸேட் மற்றும் இரத்த தட்டையணுக்கள் நிறைந்த பிளாஸ்மாவிற்கும், மெத்தோட்ரெக்ஸேட் மோனோதெரபிக்கும், வழக்கமான மேற்பூச்சு சிகிச்சைக்கும் இடைப்பட்ட மருத்துவ செயல்திறன் பற்றிய ஒப்பீட்டு ஆய்வு.

ஆய்வாளர் : மரு. யுவப்பிரியா .B

பங்கேற்பாளர் : **வயது :**

ஆராய்ச்சி மையம் : **தோல்நோய் துறை,**
இராஜீவ் காந்தி அரசு பொது மருத்துவமனை, சென்னை.

இந்த ஆய்வில் பங்கேற்பதற்காக தாங்கள் அழைக்கப்படுகிறீர்கள். இந்த ஆவணத்தில் உள்ள தகவல்கள் தாங்கள் இந்த ஆய்வில் பங்கேற்க முடிவு செய்துக் கொள்ள உதவும். இதில் ஏதேனும் சந்தேகம் இருந்தால் வெளிப்படையாக கேள்விகளைக் கேட்டு தெரிந்துக் கொள்ளலாம்.

நாங்கள் இராஜீவ் காந்தி அரசு பொது மருத்துவமனையில் தோல் நோயியல் துறையின் வெளிநோயாளிகள் பிரிவிற்கு வரும் நோயாளிகளிடையே மெத்தோட்ரெக்ஸேட் மற்றும் இரத்த தட்டையணுக்கள் நிறைந்த பிளாஸ்மாவிற்கும், மெத்தோட்ரெக்ஸேட் மோனோதெரபிக்கும், வழக்கமான மேற்பூச்சு சிகிச்சைக்கும் இடைப்பட்ட மருத்துவ செயல்திறன் பற்றிய ஆய்வு மேற்கொள்ளப்படுகிறது.

அதற்கு உங்கள் பங்களிப்பு எங்களுக்கு பெரிதும் உதவக்கூடும்.

இந்த ஆய்வின் நோக்கம்:

மெத்தோட்ரெக்ஸேட் மற்றும் இரத்த தட்டையணுக்கள் நிறைந்த பிளாஸ்மாவிற்கும், மெத்தோட்ரெக்ஸேட் மோனோதெரபிக்கும், வழக்கமான மேற்பூச்சு சிகிச்சைக்கும் இடைப்பட்ட மருத்துவ செயல்திறன் பற்றிய ஒப்பிடுதலே இந்த ஆய்வின் நோக்கமாகும்.

ஆய்வு வடிவமைப்பு: சீரற்ற கட்டுப்பாட்டு ஆய்வு

ஆய்வு முறைகள்: இந்த ஆய்வில் ஒவ்வொரு நோயாளிகளிடமும் விரிவான நோய் குறிப்புகளும் அது எவ்வளவு காலம் மற்றும் பல்வேறு நோய் வெளிப்பாடுகள் ஆகியவை குறிப்பு எடுக்கப்படும். உடலில் எந்த இடம், எந்த வடிவம் மற்றும் முழு தோல் பரிசோதனை ஆகிய மருத்துவ அம்சங்கள் இதில் எடுத்துக்கொள்ளப்படும்.

இந்த ஆய்விற்காக மருத்துவ பரிசோதனை செய்யப்பட்டு, மேலும் CBC, RFT, LFT, VCTC, VDRL, FLP, Urine Pregnancy Test, போன்ற பரிசோதனைகள் மேற்கொள்ளப்படும்.

தங்களது மருத்துவ சிகிச்சை குறித்த தகவல்கள் இரகசியமாக பாதுகாக்கப்படும். ஆய்வின் போதோ அல்லது முடிவுகளை வெளியிடும் போதோ தங்களது பெயரையோ, அடையாளங்களையோ வெளியிடமாட்டோம் என்பதை தெரிவித்துக் கொள்கிறோம்.

இந்த ஆய்வில் பங்கேற்பது உங்களுடைய விருப்பத்தின் பேரில் தான் இருக்கிறது. மேலும் நீங்கள் எந்நேரமும் இந்த ஆய்விலிருந்து பின்வாங்கலாம் என்பதையும் தெரிவித்துக் கொள்கிறோம். இந்த ஆய்வில் பங்கேற்காவிட்டாலும் நீங்கள் வழக்கமான சிகிச்சையை தொடர்ந்து பெறலாம்.

இந்த ஆய்வின் முடிவு தங்களுக்கு ஆய்வின் இறுதியிலோ அல்லது ஆய்வின் போதிலோ தெரியப்படுத்தப்படும்.

ஆய்வாளர் கையொப்பம்

பங்கேற்பாளர் / பாதுகாவலர்
கையொப்பம்

தேதி :

சுய ஒப்புதல் படிவம்

ஆராய்ச்சியின் தலைப்பு :

மெத்தோட்ரெக்ஸேட் மற்றும் இரத்த தட்டையணுக்கள் நிறைந்த பிளாஸ்மாவிற்கும், மெத்தோட்ரெக்ஸேட் மோனோதெரபிக்கும், வழக்கமான மேற்பூச்சு சிகிச்சைக்கும் இடைப்பட்ட மருத்துவ செயல்திறன் பற்றிய ஒப்பீட்டு ஆய்வு.

பெயர் : வயது : தேதி : உள்நோயாளி எண் :

..... என்பவராகிய நான் இந்த ஆய்வின் விவரங்களும் அதன் நோக்கங்களும் முழுமையாக அறிந்து கொண்டேன். எனது சந்தேகங்கள் அனைத்திற்கும் தகுந்த விளக்கம் அளிக்கப்பட்டது. இந்த ஆய்வில் முழு சுதந்திரத்துடன் மற்றும் சுயநினைவுடன் பங்கு கொள்ள சம்மதிக்கிறேன்.

எனக்கு விளக்கப்பட்ட விஷயங்களை நான் புரிந்து கொண்டு நான் எனது சம்மதத்தைத் தெரிவிக்கிறேன். இச்சுய ஒப்புதல் படிவத்தை பற்றி எனக்கு விளக்கப்பட்டது.

இந்த ஆய்வினை பற்றிய அனைத்து தகவல்களும் எனக்கு தெரிவிக்கப்பட்டது. இந்த ஆய்வில் எனது உரிமை மற்றும் பங்கினை பற்றி அறிந்து கொண்டேன்.

இந்த ஆய்வில் பிறரின் நிர்பந்தமின்றி என் சொந்த விருப்பத்தின் பேரில்தான் பங்கு பெறுகிறேன் மற்றும் நான் இந்த ஆராய்ச்சியிலிருந்து எந்நேரமும் பின் வாங்கலாம் என்பதையும் அதனால் எந்த பாதிப்பும் ஏற்படாது என்பதையும் நான் புரிந்து கொண்டேன்.

இந்த ஆய்வில் கலந்து கொள்வதன் மூலம் என்னிடம் பெறப்படும் தகவலை ஆய்வாளர் இன்ஸ்டிட்யூசனல் எத்திக்ஸ் கமிட்டியினரிடமோ, அரசு நிறுவனத்திடமோ தேவைப்பட்டால் பகிர்ந்து கொள்ளலாம் என சம்மதிக்கிறேன்.

இந்த ஆய்வின் முடிவுகளை வெளியிடும்போது எனது பெயரோ, அடையாளமோ வெளியிடப்பட்டாது என அறிந்து கொண்டேன். இந்த ஆய்வின் விவரங்களைக் கொண்ட தகவல் தாளைப் பெற்று கொண்டேன்.

இந்த ஆய்விற்காக மருத்துவ பரிசோதனை செய்யப்பட்டு CBC, RFT, LFT, VCTC, VDRL, FLP, Urine Pregnancy Test போன்ற பரிசோதனைகள் செய்து கொள்ள சம்மதிக்கிறேன்.

இந்த ஆய்வில் பங்கேற்கும் பொழுது ஏதேனும் சந்தேகம் ஏற்பட்டால், உடனே ஆய்வாளரை தொடர்பு கொள்ள வேண்டும் என அறிந்து கொண்டேன்.

இச்சுய ஒப்புதல் படிவத்தில் கையெழுத்திடுவதன் மூலம் இதிலுள்ள அனைத்து விஷயங்களும் எனக்கு தெளிவாக விளக்கப்பட்டது என்றும் தெரிவிக்கிறேன் என்று புரிந்து கொண்டேன். இச்சுய ஒப்புதல் படிவத்தின் ஒரு நகல் எனக்கு கொடுக்கப்படும் என்றும் தெரிந்து கொண்டேன்.

பங்கேற்பாளர் / பாதுகாவலர் கையொப்பம் தேதி :

ஆய்வாளர் கையொப்பம் தேதி :

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI 600 003

EC Reg.No.ECR/270/Inst./TN/2013/RR-16
Telephone No.044 25305301
Fax: 011 25363970

CERTIFICATE OF APPROVAL

To
Dr.**B.YUVA PRIYA,**
First year MD DVL,
Department of Dermatology
Madras Medical College & RGGGH,
Chennai-600003.

Dear Dr. B.YUVA PRIYA,

The Institutional Ethics Committee has considered your request and approved your study titled **"A COMPARATIVE STUDY ON CLINICAL EFFICACY OF PALTELET RICH PLASMA IN COMBINATION WITH METHOTREXATE VERSUS METHOTREXATE MONOTHERAPY VERSUS CONVENTIONAL TOPICAL THERAPY IN CHRONIC PLAQUE PSORIASIS"-NO.13112019.** The following members of Ethics Committee were present in the meeting held on **05.11.2019** conducted at Madras Medical College, Chennai 3.

1. Prof.P.V.Jayashankar :Chairperson
2. Prof.R.Jayanthi,MD.,FRCP(Glasg)., Dean,MMC,Ch-3 :DeputyChairperson
3. Prof.N.Gopalakrishnan,MD.,DM.,FRCP, Vice Principal Director,Inst.of Nephrology,MMC,Ch : Member Secretary
4. Prof.Bharathi Vidya Jayanthi,Vice Principal Director,Inst. of Pathology,MMC,Ch- : Member
5. Prof.R.Muthuselvan,MD,Prof. Inst. of Int.Med,MMC, Ch-3 : Member
6. Prof.Alli, Prof. Inst. of Gen.Surgery,MMC : Member
7. Prof.Shobha, Prof, Inst.of O&G, Chennai : Member
8. Prof.Rema Chandramohan,Prof.of Paediatrics,ICH,Chennai : Member
9. Prof. Sudha, Prof. Inst. of Pharmacology,MMC,Ch-3 : Member
10. Prof.K.Ramadevi,MD., Director, Inst. of Bio-Chemistry,MMC,Ch-3 : Member
11. Prof. S.Lakshmi, Prof. of Paediatrics ICH Chennai : Lawyer
12. Thiru S.Govindasamy, BA.,BL,High Court,Chennai :Social Scientist
13. Tmt.Arnold Saulina, MA.,MSW., : Lay Person
14. Thiru K.Ranjith, Ch- 91

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

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 the protocol and patients information/informed consent and asks to be provided a copy of the final report.

Member Secretary – Ethics Committee

Curiginal

Document Information

Analyzed document	A comparative study on clinical efficacy of PRP, methotrexate and topcal therapy in psoriasis vulgaris.docx (D123341988)
Submitted	2021-12-21T11:24:00.0000000
Submitted by	Yuva priya B
Submitter email	yuvapriya271@gmail.com
Similarity	3%
Analysis address	yuvapriya271.mgrmu@analysis.urkund.com

PLAGIARISM CERTIFICATE

This is to certify that this dissertation work titled **"A COMPARATIVE STUDY ON CLINICAL EFFICACY OF PLATELET RICH PLASMA IN COMBINATION WITH METHOTREXATE VERSUS METHOTREXATE MONOTHERAPY VERSUS CONVENTIONAL TOPICAL THERAPY IN CHRONIC PLAQUE PSORIASIS"** of the candidate **Dr. YUVA PRIYA .B** with registration Number **201930027** for the award of **M.D, Dermatology, Venereology & Leprosy** in the branch of **XX**. I personally verified the urkund.com website for the purpose of plagiarism Check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows **3 percentage** of plagiarism in the dissertation.

Guide & Supervisor sign with Seal.

MASTER CHART - GROUP A

Name	Age	Sex	Duration	Site	Co morbidity	Personal history	CBC	RFT	LFT	Group	Pre treatment PASI	After 1 month	After 2 months	After 3 months	Results at 1st month	Results at 2nd month	Results at 3 month	Overall result	Adverse effects	Recurrence
Beula	40	Female	6 months	LL	nil	nil	normal	normal	normal	1-PRP	3.2	3.2	2.6	2	No change	improved	improved	improved	Pain	nil
Kathiresan	67	Male	9 months	Palmo plantar	nil	nil	normal	RBS	normal	1-PRP	4	3.2	1.6	1.6	improved	improved	improved	improved	Pain	nil
Balachandran	48	Male	2 years	LL	nil	nil	normal	normal	normal	1-PRP	2.4	2.4	2.4	2.4	No change	No change	No change	no change	Nil	nil
Stella	42	Female	1 year 8 months	LL	Asthma	nil	normal	normal	normal	1-PRP	3.2	3.2	2	2	No change	improved	improved	improved	Pain	nil
Rani	32	Female	2 years	LL	nil	nil	normal	normal	normal	1-PRP	3.2	3.2	3.2	3.2	No change	No change	No change	no change	Nil	lost follow up
Umarani	50	Female	6 years 4 months	LL	DM	nil	normal	RBS	normal	1-PRP	2.4	2.4	2	1.2	No change	improved	improved	improved	Nil	nil
Jansirani	38	Female	6 years	UL	nil	nil	normal	normal	normal	1-PRP	2.4	2.4	2.4	2.4	No change	No change	No change	no change	Pain	nil
Vasanthi	44	Female	2 years	LL	nil	nil	normal	normal	normal	1-PRP	3.2	3.2	2.4	2	No change	No change	improved	improved	Nil	lost follow up
Aanandan	59	Male	9 months	LL	Asthma	nil	normal	normal	normal	1-PRP	2.8	2.8	2.8	2.8	No change	No change	No change	no change	Pain	nil
Selvaganapathy	37	Male	1 year	UL	nil	nil	normal	normal	normal	1-PRP	2.8	2.8	2.8	2	No change	No change	improved	improved	Nil	nil
Jayarani	49	Female	2 years	Palmo plantar	nil	nil	normal	normal	normal	1-PRP	4.2	3.6	3.6	2	improved	improved	improved	improved	Irritation	yes
Selvamani	40	Female	10 years	LL	nil	nil	normal	normal	normal	1-PRP	3.2	3.2	2.6	2	No change	improved	improved	improved	Nil	lost follow up
Ragavendran	34	Male	11 months	trunk	nil	nil	normal	normal	normal	1-PRP	7.2	7.2	6.8	5.4	No change	improved	improved	improved	Nil	nil
Majendran	53	Female	2 years	LL	nil	smoker	normal	normal	normal	1-PRP	2.4	2.4	2.4	2	No change	No change	improved	improved	Nil	yes
Mani	55	Male	8 months	LL	nil	nil	normal	normal	normal	1-PRP	3.2	3.2	2.6	2	No change	No change	improved	improved	Pain	nil
Baskar	37	Male	3 years	UL	nil	nil	normal	normal	normal	1-PRP	3.2	3.2	3.2	3.2	No change	No change	No change	no change	Nil	nil
Sambosivarao	67	Male	3 years	LL	DM	alcoholic	normal	normal	normal	1-PRP	5.6	5.6	4.2	4.2	No change	improved	improved	improved	Nil	nil
Ramaye	52	Female	1 year	LL	nil	nil	normal	normal	normal	1-PRP	2.4	2.4	2.4	2	No change	No change	improved	improved	Nil	lost follow up
Bakrudheen	43	Male	8 months	trunk	nil	nil	normal	normal	normal	1-PRP	4.4	3.2	2.8	2	improved	improved	improved	improved	Pain	nil
Prema	60	Female	2 years	LL	HT	nil	normal	normal	normal	1-PRP	3.6	3.6	3.6	3.6	No change	No change	No change	no change	Nil	lost follow up
Venkadeshan	55	Male	1 year	UL	nil	nil	normal	normal	normal	1-PRP	2.8	2.8	2	1.6	No change	improved	improved	improved	Nil	nil
Ravi	54	Male	4 years 8 months	LL	nil	nil	normal	normal	normal	1-PRP	3.2	3.2	1.6	1.6	No change	improved	improved	improved	Nil	nil

MASTER CHART - GROUP B

Name	Age	Sex	Duration	Site	Co morbidity	Personal history	CBC	RFT	LFT	Group	Pre treatment PASI	After 1 month	After 2 months	After 3 months	Results at 1st month	Results at 2nd month	Results at 3 month	Overall result	Adverse effects	Recurrence
Mahalakshmi	52	Female	16 months	LL, trunk	nil	nil	normal	normal	normal	2-MTX	2.8	2.8	2.8	2.8	No change	No change	No change	No change	Nil	nil
Karthick	38	Male	2 years	LL	nil	nil	normal	normal	normal	2-MTX	4.8	4.8	4.8	3.2	No change	No change	improved	improved	Nil	nil
Sameena	49	Female	5 months	LL	nil	nil	normal	normal	normal	2-MTX	2.4	2.4	2.4	2.4	No change	No change	No change	No change	Nil	nil
Karthikeyan	71	Male	4 years	LL	nil	smoker	normal	normal	normal	2-MTX	3.2	3.2	2.4	2.4	No change	improved	improved	improved	Nil	yes
Sridhar	50	Male	1 year 3 months	LL	nil	nil	normal	normal	normal	2-MTX	3.2	3.2	3.2	3.2	No change	No change	No change	No change	Nil	lost follow up
Rakkir	78	Male	2 years 4 months	LL	HT	nil	normal	normal	normal	2-MTX	2.8	2.8	2.8	2.8	No change	No change	No change	No change	Nil	nil
Sathish	44	Male	6 months	UL	nil	nil	normal	normal	normal	2-MTX	1.6	1.6	1.6	1.6	No change	No change	No change	No change	Pain	nil
Rakkir	58	Male	4 years	LL	nil	nil	normal	normal	normal	2-MTX	3.2	3.2	2.4	2	No change	improved	improved	improved	Nil	lost follow up
Sathish	44	Male	2 years	UL	nil	nil	normal	normal	normal	2-MTX	3.6	3.6	3.6	3.6	No change	No change	No change	No change	Pain	nil
Sakita	70	Female	8 months	LL	DM	nil	normal	normal	normal	2-MTX	4.2	4.2	4.2	4.2	No change	No change	No change	No change	Nil	nil
Vijaya Lakshmi	55	Female	2 years 9months	LL	nil	nil	normal	normal	normal	2-MTX	2.8	2.8	2.8	2.8	No change	No change	No change	No change	Nil	lost follow up
Alex	51	Male	3 years	LL	nil	smoker & alcoholic	normal	normal	normal	2-MTX	3.2	3.2	2.6	2.4	No change	improved	improved	improved	Nil	lost follow up
Pratap kumar	55	Male	5 years	trunk	nil	nil	normal	normal	normal	2-MTX	4.8	4.8	4.8	4.8	No change	No change	No change	No change	Irritation	nil
Kandjasamy	64	Male	1 year	LL	HT	alcoholic	normal	normal	normal	2-MTX	2.4	2.4	2.4	2	No change	No change	improved	improved	Nil	yes
Madhankumar	27	Male	6 months	LL	nil	nil	normal	normal	normal	2-MTX	2.8	2.8	2.6	2.6	No change	improved	No change	No change	Nil	nil
Balaji	45	Male	10 months	LL	nil	nil	normal	normal	normal	2-MTX	3.2	3.2	3.2	3.2	No change	No change	No change	No change	Nil	nil
Vimala	30	Female	2 years	LL	nil	nil	normal	normal	normal	2-MTX	4.2	4.2	4.2	4.2	No change	No change	No change	No change	Nil	nil
Ramdoss	80	Male	5 years	LL	nil	nil	normal	normal	normal	2-MTX	2.8	2.8	2.8	2.8	No change	No change	No change	No change	pain	nil
Chellappa	58	Male	1 year	Palmo plantar	nil	smoker	normal	normal	normal	2-MTX	4.2	3.2	2.8	2	improved	improved	improved	improved	Nil	yes
Kabirdoss	71	Male	11 months	LL	DM	nil	normal	normal	normal	2-MTX	5.6	5.6	5.6	5.6	No change	No change	No change	No change	Nil	lost follow up
Sundaralakshmi	40	Female	3 years	LL	nil	nil	normal	normal	normal	2-MTX	2.8	2.8	2	1.6	No change	improved	improved	improved	Nil	nil
Srividhya	42	Female	1 year 2 months	UL	nil	nil	normal	normal	normal	2-MTX	3.2	3.2	3.2	3.2	No change	No change	No change	No change	Nil	nil

MASTER CHART - GROUP C

Name	Age	Sex	Duration	Site	Co morbidity	Personal history	CBC	RFT	LFT	Group	Pre treatment PASI	After 1 month	After 2 months	After 3 months	Results at 1st month	Results at 2nd month	Results at 3 month	Overall result	Adverse effects	Recurrence
Sivabalan	45	Male	2 years	trunk	nil	nil	normal	normal	normal	3-TOPICAL	3.2	3.2	2.6	2	No change	improved	improved	improved	Nil	nil
Baby	64	Female	9 months	LL	nil	nil	normal	normal	normal	3-TOPICAL	3.2	3.2	3.2	3.2	No change	No change	No change	No change	Nil	nil
Nirmalarani	57	Female	4 years	LL	DM	nil	normal	normal	normal	3-TOPICAL	2.8	2.4	2.4	2.4	improved	No change	No change	improved	Nil	nil
Saaikala	60	Female	7 years	UL	nil	nil	normal	normal	normal	3-TOPICAL	3.6	3.6	3.6	3.6	No change	No change	No change	No change	depigmentation	lost follow up
Jeevarathinam	49	Male	6 months	trunk	nil	smoker	normal	normal	normal	3-TOPICAL	4.2	4.2	3.2	3.2	No change	improved	No change	improved	Nil	yes
Rajendtan	59	Male	3 years	LL	DM	nil	normal	normal	normal	3-TOPICAL	2.4	2.4	2	1.2	No change	improved	improved	improved	Nil	nil
Amala	39	Female	1 year	LL	nil	nil	normal	normal	normal	3-TOPICAL	2.4	1.6	1.6	1.2	improved	No change	improved	improved	Nil	lost follow up
Ramanibhai	50	Female	1 year 6 months	UL	nil	nil	normal	normal	normal	3-TOPICAL	3.2	3.2	3.2	3.2	No change	No change	No change	No change	Nil	nil
Gajapathy	53	Male	3 years	LL	nil	alcoholic	normal	normal	normal	3-TOPICAL	2.8	2.8	2.8	2.8	No change	No change	No change	No change	Nil	nil
Valarmathi	42	Female	6 months	LL	nil	nil	normal	normal	normal	3-TOPICAL	5.6	5.6	5.6	4.8	No change	No change	improved	improved	Nil	yes
Jeyanth	30	Male	2 years	UL	nil	nil	normal	normal	normal	3-TOPICAL	2.8	2	1.6	1.6	improved	improved	No change	improved	Nil	yes
Nagaraja	46	Male	8 months	LL	nil	nil	normal	normal	normal	3-TOPICAL	3.2	3.2	3.2	3.2	No change	No change	No change	No change	Nil	nil
Kathirvel	60	Male	3 years	LL	HT	Smoker & alcoholic	normal	normal	normal	3-TOPICAL	4.8	4.8	3.2	3.2	No change	improved	No change	improved	Nil	lost follow up
Josphine	58	Female	9 months	UL	nil	nil	normal	normal	normal	3-TOPICAL	3.2	3.2	3.2	2.4	No change	No change	improved	improved	Nil	nil
Mangalam	45	Female	14 months	UL	nil	nil	normal	normal	normal	3-TOPICAL	4.2	4.2	4.2	4.2	No change	No change	No change	No change	Nil	nil
Jayalakshmi	60	Female	5 years	LL	nil	nil	normal	normal	normal	3-TOPICAL	3.2	3.2	3.2	3.2	No change	No change	No change	No change	Nil	nil
Latha	56	Female	1 year	LL	nil	nil	normal	normal	normal	3-TOPICAL	2.8	2.8	2.8	2.8	No change	No change	No change	No change	Nil	lost follow up
Chinnaponnu	60	Female	3 years	UL	DM	nil	normal	normal	normal	3-TOPICAL	2.4	2.4	2.4	2	No change	No change	improved	improved	depigmentation	nil
Maragathavalli	43	Female	1 year 8 months	trunk	nil	nil	normal	normal	normal	3-TOPICAL	6.6	6.6	6.2	5	No change	improved	improved	improved	Nil	yes
Arumugam	60	Male	5 years	LL	nil	smoker	normal	normal	normal	3-TOPICAL	3.6	3.6	3.6	2.4	No change	No change	improved	improved	Nil	nil
Ragavan	49	Male	6 months	LL	nil	nil	normal	normal	normal	3-TOPICAL	2.8	2.8	2.8	2.8	No change	No change	No change	No change	Nil	nil
Elisabeth	57	Female	1 4 months	trunk	nil	nil	normal	normal	normal	3-TOPICAL	3.2	3.2	2.8	2	No change	improved	improved	improved	Nil	yes