International Journal of Life Sciences, Biotechnology and Pharma Research Vol. 13, No. 9, September 2024 Online ISSN: 2250-3137
Print ISSN: 2977-0122

DOI: 10.69605/ijlbpr_13.9.2024.44

REVIEW ARTICLE

Clinical efficacy and safety of combination of topical vitamin D analogues and Clobetasol in psoriasis vulgaris: A systematic review

Dr. Suniti T. Upalekar[1], Dr. Anagha P. Marawar[2], Dr. Vaishali Praful Bansod[3]

[1]Assistant Professor, [2]Professor and head of department, Department of Pharmacology**,** Bharatratna Atal Bihari Vajpayee Medical College & Hospital, Mangalwar Peth, Pune, Maharashtra, India
[3]Assistant Professor, Department of Community Medicine, Bharatratna Atal Bihari Vajpayee Medical College, Mangalwar Peth, Pune, Maharashtra, India

Corresponding author
Dr. Vaishali Praful Bansod
Assistant Professor, Department of Community Medicine, Bharatratna Atal Bihari Vajpayee Medical College, Mangalwar Peth, Pune, Maharashtra, India
Email: vaishalibansod63@gmail.com

Received Date: 21 July, 2024 Acceptance Date: 24 August, 2024

ABSTRACT

Topical combination of clobetasol propionate and vitamin D analogues have been commonly used to treat psoriasis vulgaris. However, there is no consolidated information regarding its efficacy and safety.Randomized controlled trials on psoriasis vulgaris using the combination weresearched onPubMed, PubMed Central, and Medline.4 randomized controlled trials with870 participants were included. The trials used topical clobetasol propionate and vitamin D analogues for 6- 26 weeks and were compared withonly vit D analogue or vitamin D analogue / vehicle or vitamin D analogue /betamethasone or only clobetasol propionate.In the first study after 2 weeks treatment with clobetasol propionate and 4 weeks treatment with calcipotriol showed significantly lower overall severity score. ($p < 0.0001$) than 6 weeks continuous treatment with calcipotriol. In the second study combination is more effective as compared to calcipotriol/vehicle group. ($p=0.02$).In the third study theoverall severity score at week 2 was significantly lower for combination therapy group as compared to either monotherapy groups ($p=0.0017$, $p < 0.0001$). In the fourth study both the treatment modalities like excimer and calcipotriol-clobetasol combination showed significant reduction in MPPPASI score. (0.002)Topical application of clobetasol and vitamin D analogue is more effective in combination as compared to monotherapy with mild adverse events.

Keywords: Clinical efficacy, vitamin D analogues, Clobetasol, psoriasis vulgaris, a systematic review

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution- Non Commercial-Share Alike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

INTRODUCTION

Psoriasis is a common,chronic,and recurrent inflammatory dermatosischaracterized clinically by silvery white scaly lesions on erythematous base,and histologically by epidermal proliferation and dermal inflammation.It affects predominantly the extensor areas and pressure areas such as knee,elbow or scalp and also palms,soles,umbilicus and glans penis.[1]

In USA the prevalence of psoriasis was estimated to be around 4.6% while in Canada it was found to be 4.7%.InIndia the incidence of psoriasis among total skin patients ranged between 0.44% and 2.2% and prevalence varies from 0.44 to 2.8%. [2]

Psoriasis not only affects patient'squality of life andhas psychologicaleffects including depression, alexithymia,coping with feelings of stigmatization and suicide ideation.[3]Psoriasis has genetic predisposition and there is increased susceptibility in first degree relatives.There are certain environmental triggers for psoriasis such as drug intake,infections,trauma,smoking,alcohol and stress.Streptococcal throat infection,Vitamin D Deficiency,direct skin trauma can also trigger psoriasis.[4]

Psoriasismanifests in different forms such as chronic plaque psoriasis,guttate psoriasis,generalized pustular psoriasis,psoriatic erythroderma and inverse/flexural psoriasis.Nail psoriasis can affect about 40% of patients of psoriasis.Psoriasis is associated with comorbidities like increased risk of chronic kidney disease,non-alcoholic fatty liver disease,coronary artery disease,obstructive sleep apnea,chronic

©2024Int. J. LifeSci.Biotechnol.Pharma.Res.

DOI: 10.69605/ijlbpr_13.9.2024.44

obstructive pulmonary disease,inflammatorybowel disease and psychiatric comorbidities.[4]

The severity of psoriasis is evaluated by scores such as Body surface areaassessment,Psoriasis Area Severity Index,Dermatology Life Quality Index and Psoriasis Disability Index.[4]Psoriasis is an autoimmune disease with activation of parts of immune system. The keratinocytes, dendritic cells and T cells are in a chronic inflammatory state due to production of cytokines.[5]

In Psoriasis the antigen attaches to the major histocompatibility complex (MHC) of antigen presenting cells (APC). Antigen-bound APC migrates to lymph nodes. Antigens are presented to T cells and co-stimulation via APC. The activated T cell clones are redirected to blood vessels through which they reach the epidermis. The T cells releases cytokines. Hyperstimulation by cytokines leads to the formation of hyperkeratotic psoriatic skin.[5](refer figure 1)

Topical medications are the most commonly used agents to treat mild to moderate psoriasis.They are frequently used as adjunctive therapies for patients on phototherapy,systematic or biologic therapy.[6]Commonly used topical medicationsinclude salicylic acid,urea,tazarotene,tar,anthracene,glucocorticoid and vitamin D analogues.[7]

Topical steroids are very effective agents used in the therapeutic management of psoriasis. Steroidal formulations are divided into 4 groups as per therapeutic potential as mild, moderate, potent and super potent. Topical corticosteroids are used early in the treatment of psoriasis especially when the body surface area affected is limited. Clobetasol propionate belongs to the strongest group that is super potent group and has been FDA approved in November 1996 for treatment of psoriasis.[8,9]

Topical corticosteroids however cannot be used in certain areas such as face, genital and inguinal region or when they have to be applied to large surface area for prolonged duration and cannot be used in children. Super potent corticosteroids are used in approximately 60% patients of plaque psoriasis and are better than agents of lesser potency in achieving initial clearance and marked improvement. Clobetasol propionate induces rapid healing of psoriasis. Clobetasol propionate 0.025% is as efficacious and safer than clobetasol propionate 0.05% formulation.[8]

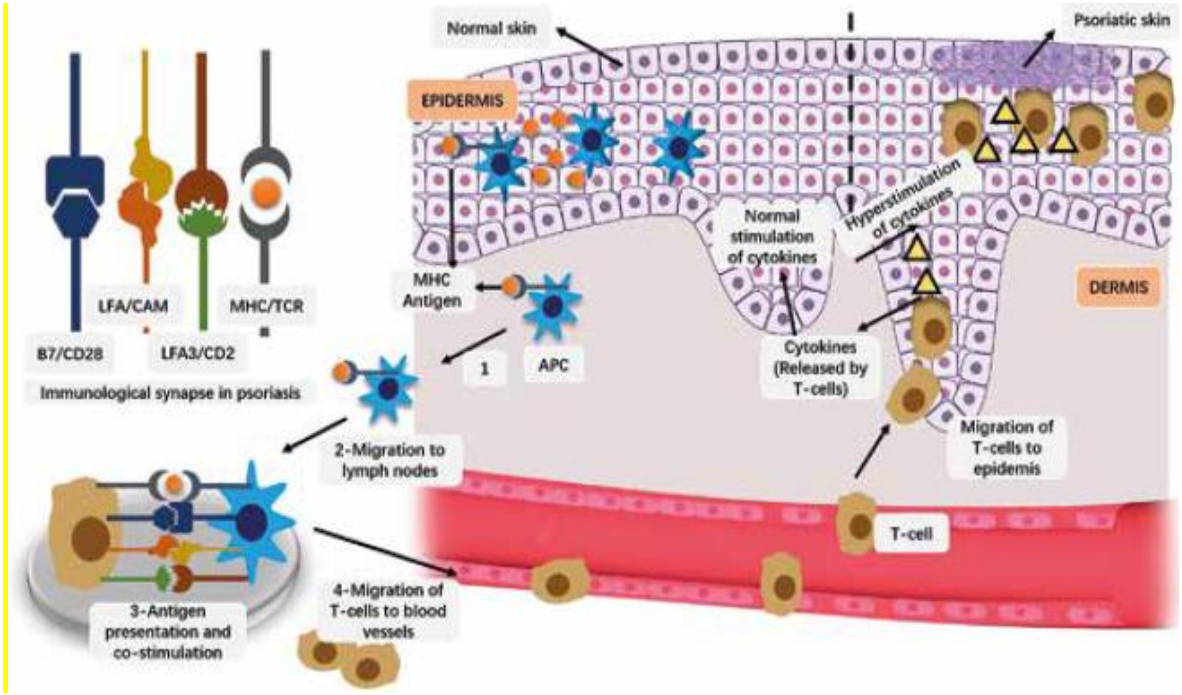

Figure 1: Basic Pathological events involved in psoriasis[5]

Mechanism of action

Clobetasol propionate acts by two pathways at cellular level (genomic pathway and non-genomic pathway).In the genomic pathway clobetasol binds to intracellular cytoplasmic corticosteroid receptor which migrates to the nucleus and binds to glucocorticoid response element which regulates transcription of numerous genes particularly those that code for pro inflammatory cytokines.[9](refer figure 2)

In an unbound state intracellular glucocorticoid receptor is bound to immunophilin and to heat shock protein 90. After steroid binding, the steroid glucocorticoid receptor complex binds with the dynein protein translocating the complex from cytoplasm to nucleus. There is promotion of anti-inflammatory functions (phosphoenol pyruvate carboxykinase (PEPCK), dual specificity protein phosphatase 1(DUSP 1), tyrosine amino transferase (TAT), Beta adrenergic receptor, IL 10, and IL 1 receptor antagonist) after transcription of genes. There is either stimulation or repression of transcription of genes resulting in variation of m RNA synthesis and

©2024Int. J. LifeSci.Biotechnol.Pharma.Res.

DOI: 10.69605/ijlbpr_13.9.2024.44

protein synthesis. Clobetasol propionate decreases proliferation of T lymphocytes, formation of arachidonic acid metabolic products, suppresses cytokine expression and effects.[9]

Thus, clobetasol propionate has vasoconstrictive, anti-proliferative, anti-inflammatory and immunosuppressive properties.[10]

The non-genomic pathway gives rise to immediate therapeutic effect. There is modulation of activation levels and the response of target cells that is monocytes, platelets and T cells.[9]

Thedifficulties encountered with topical corticosteroid therapy include adverse reactions associated with prolonged continuous use such as cutaneous atrophy,striae,persistent erythema, telangiectasia and tachyphylaxis. Tachyphylaxis describes a reduced therapeutic effect despite continued application, which may be due to a true loss of efficacy, poor adherence, or both. There is a potential systematic side effect associated with prolonged steroid use that is hypothalamo-pituitary axis suppression which occurs when a high potency steroid is used over large surface area for prolonged duration.[(11,12)]

As psoriasis recurs after stopping treatment with steroid,steroid sparing agents such as vitamin D analogues have been developed to supplement and reduce over reliance on topical corticosteroids.[4]The immunosuppressiveeffects of corticosteroids are critical for inhibiting the pro-inflammatory environment and T-cell activation. Vitamin D analogues exert normalizing effects on the hyperproliferation and abnormal differentiation of keratinocytes and also have immunomodulatory effects. Corticosteroid and vitamin D analogue monotherapy is associated with increased risks of skin atrophy and perilesional skin irritation,respectively. Long-term continuous use of topical corticosteroid treatment alone can lead to skinatrophy. As a result, the thickness of the skin is reduced and trans epidermal water loss increases,causing loss of skin barrier function. Recent studies in cultured skin cells have demonstrated that the addition of calcipotriol reduces the early signs of betamethasone and clobetasol-induced skin atrophy by modulating key ECM components.[3]Systematic adverse effects like hypercalcemia and parathyroid hormone suppression are quite rare. [4]

Vitamin D analogues have been used topically singly as monotherapy or in combination with corticosteroids in psoriasis. They are particularly helpful in hard to treat areas such as face and inguinal region.[13]They are also used to treat nail psoriasis and chronic plaque psoriasis of scalp.[14]They unlike corticosteroids do not exhibit tachyphylaxis and can be used indefinitely without serious side effects. They are effective in treating children and elderly. They are comparable in efficacy to corticosteroids.[15]

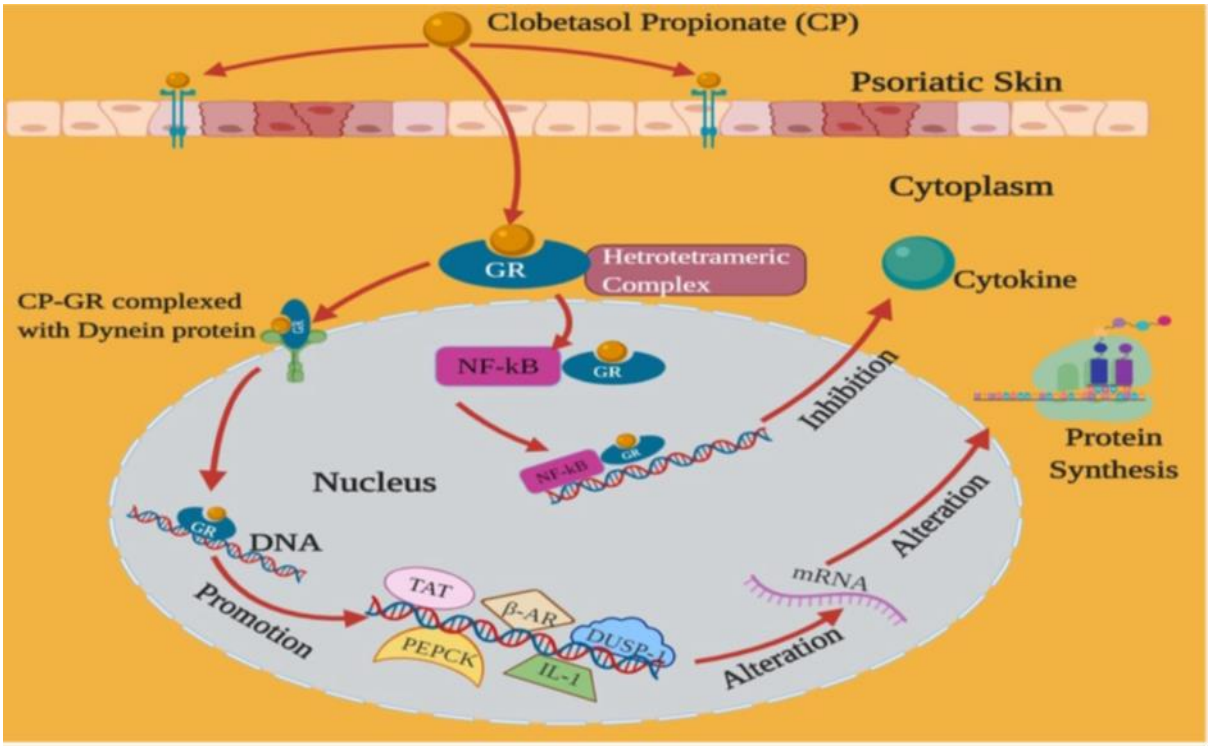

Figure 2: Mechanism of action of clobetasol propionate after topical application [9]

GR—Glucocorticoid Receptor; TAT—tyrosine aminotransferase; PEPCK—phosphoenolpyruvate carboxykinase; AR—beta-adrenergic receptor; DUSP—dual-specificity protein phosphate; NF-nuclear factor; kappa-light-chain-enhancer; IL-1—interleukin 1; mRNA—messenger RNA.

©2024Int. J. LifeSci.Biotechnol.Pharma.Res.

DOI: 10.69605/ijlbpr_13.9.2024.44

Mechanism of action

The therapeutic effect is seen by binding to intracellular vitamin D receptor and binding and regulation of VDR mediated genomic mechanism inhibiting keratinocyte proliferation and non-genomic mechanisms causing keratinocyte differentiation through raised calcium levels. They exhibit anti-inflammatory mechanism through inhibition of IL 2 and IL6 and INF ɣ. Vitamin D analogues also inhibit human β defensins and pro inflammatory cytokines found in increased amounts in psoriatic lesions.[15]

Calcipotriene is a synthetic analogue of vitamin D and is one of the most commonly prescribed medications for the treatment of psoriasis.[2]It was also the first vitamin D3 analogue to be used in psoriasis. Subsequently, calcitriol and tacalcitol were developed as were maxacalcitol and tisocalcitate more recently.[6]

Researchers worldwide have conducted a number of clinical trials to study the safety and efficacy of clobetasol and vitamin D analogues either in combination or separately or one followed by the other.Thereis no article conductingsystematic review of the combination of clobetasol with vitamin D analogues.This study aims to evaluate efficacy and safety of combination use of clobetasoland vitamin D analogues and comparing the same with clobetasol propionate alone or vitamin D analogue or placebo or excimer laser in the treatment of different forms of psoriasis by performing a systematic review.

MATERIAL AND METHODS

The study is conducted according to the Prisma statement 2020.The study is based on previously conducted studies and does not involve any animals or human experiments

Data sources and Search strategy: A search was conducted from 5th February 2023 using PubMed,PubMed Central,and Medline and was based on the guidelines of preferred reporting items for Systematic Review and Meta-Analysis (PRISMA). The search strategy consists of the following keywords and mesh terms. Psoriasis vulgaris or Palmoplantar psoriasis or scalp psoriasis or Nail psoriasis or ("Psoriasis/drug therapy"[Majr] OR "Psoriasis/therapy"[Majr]) AND Vitamin D analogues or Calcipotriol or Calcipotriene or Tacalcitol or ("Calcitriol/administration and dosage"[Majr] OR "Calcitriol/adverse effects"[Majr] OR"Calcitriol/therapeutic use"[Majr] OR "Calcitriol/toxicity"[Majr]) AND Steroid or clobetasol propionate or "Clobetasol/administration and dosage"[Majr] OR "Clobetasol/adverse effects"[Majr] OR "Clobetasol/therapeutic use"[Majr] OR "Clobetasol/toxicity"[Majr]). The search strategy was limited to English language only.

Eligibility Criteria

Inclusion Criteria: Studies assessing the effects of vitamin D analog, and Clobetasol propionate in psoriasis vulgaris with Placebo or any other intervention as the comparison group were included in the review. Only Randomized Control Trials (RCT) published in any year with full text article were included in the review.

Exclusion Criteria: Studies on animals, pediatric population, reviews, case reports, comments, abstracts, conference proceeding and studies with incomplete data were excluded from the review.

Study selection and data extraction: Articles were searched with the mentioned search strategy by two reviewers independently and articles were transferred to Excel sheet to remove duplicates. Titles and abstracts of articles were scanned for inclusion and exclusion criteria. Information about type of publishing country and date, study area, study population, selection criteria, study design, patient's allocation to groups, blinding method, doses and duration of treatment,number of patients, interventions done, and study findingswere tabulated. Systematic review focused on outcome indicators likePsoriasis and Area Severity Index (PASI) score, Modified Palmoplantar pustular Psoriasis area and Severity Index (mPPPASI) score,Investigator Global Severity assessment of psoriasis, Subject Severity assessment of Psoriasis.

Quality assessment: Quality assessment for selected RCTs was conducted by two reviewers independently using Cochrane risk of bias tool and PRISMA 2020 guidelines and disagreement if any was resolved by a third reviewer. Risk of bias was assessed in sequence generation, allocation concealment, blinding, completeness of data and selective outcome reporting.

RESULTS AND DISCUSSION

Eligible studies

Total 4 studies were identified after systematic literature search. With search strategy on pubmed, total 5077 studies were found. After filter for clinical trial, 3919 were excluded. 31 were excluded on applying filter for RCT & English. After screening for title, 1115 were excluded. 8 studies were excluded after screening for open label study and full text article. (refer figure 3)

©2024Int. J. LifeSci.Biotechnol.Pharma.Res.

DOI: 10.69605/ijlbpr_13.9.2024.44

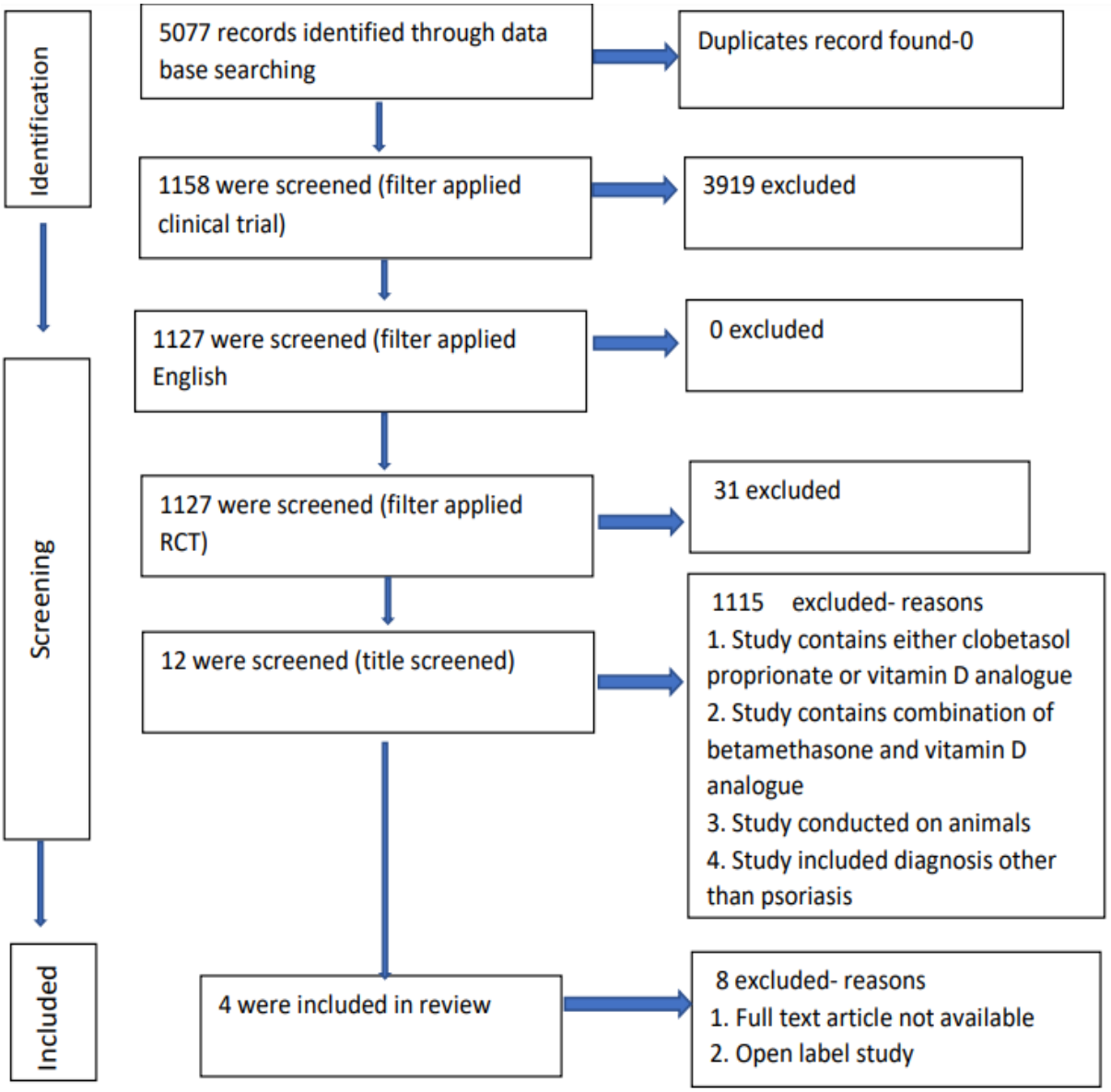

Figure 3: The flowchart of the study selection process

Risk of bias assessment and study characteristics

All studies reported the random allocation of the study participants. Only one study described the method of randomization. Two studies mentioned about blinding of participants and researchers. One study reported blinding of only participants. One study did not mentionabout blinding. (refer figure 4 and 5)Total 870 participants with psoriasis vulgaris were included in the systematic review. The duration of treatment ranged from 8 weeks to 26weeks. The characteristics of studies included are shown in table 1.

©2024Int. J. LifeSci.Biotechnol.Pharma.Res.

DOI: 10.69605/ijlbpr_13.9.2024.44

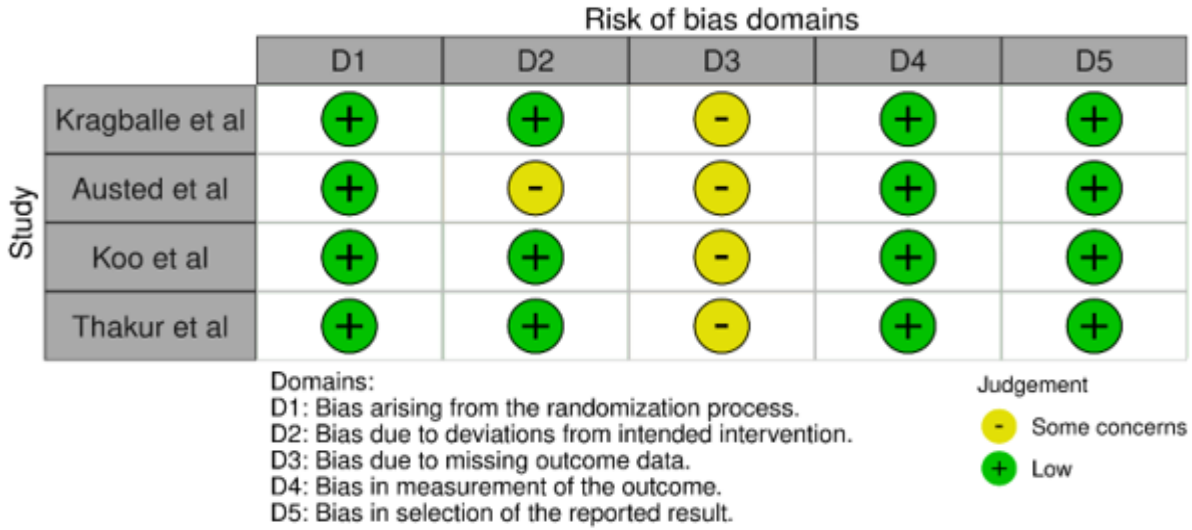

Figure 4: ROB 2 traffic-light plot displaying quality checks for RCTs

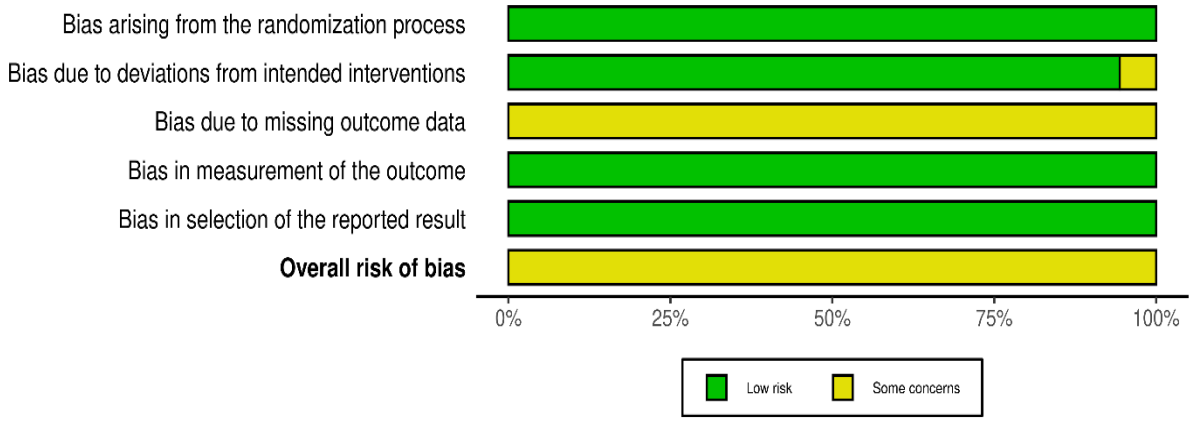

Figure 5: ROB 2 bar plot displaying quality check for RCTs

Table 1: Characteristics of included studies

Author, year	Country of origin	Duration	Number of patients	Intervention	Population of interest	Reported Adverse events	Analysis method used and Findings
Austad et al (1998)[18]	Norway	6 weeks of treatment with 4 weeks of post cessation observation	49	4 weeks washout phase with Clobetasol propionate 0.05% BD for 2 weeks followed by Calcipotriol 50mcg/g BD for 4 weeks on one side of body **(group 1)** compared with 6 weeks continuous	Patients age 18-68 years with Moderate to severe stable plaque psoriasis with mean psoriasis duration 15.6 years	Four patients reported adverse events like increased skin irritation, pruritis, reddish discoloration, influenza and bronchitis. No rebound effect was seen after	1.Median overall severity score At 2 weeks was significantly lower for clobetasol propionate than calcipotriol (P<0.0001). After subsequent 4 weeks the severity for lesions treated in **group 1** was significantly lower than **group 2.** (P<0.0001) Score for individual sign of erythema, thickness, scaling and pruritus had same

©2024Int. J. LifeSci.Biotechnol.Pharma.Res.

DOI: 10.69605/ijlbpr_13.9.2024.44

				treatment with Calcipotriol 50mcg/g BD on other side of body **(group 2)**		cessation of treatment for 4 weeks observation period	pattern in both the groups. 2.As per Physician's global assessment of treatment, they favoured group 1 as compared to group 2 for treatment difference (p-0.001) 3.Median severity score was 3 for group 1 and 3.5 for group2. 4. In 4 weeks observation period, Physician's global assessment of treatment, favoured group1 as compared to group 2. (p-0.008)
Kragballe et al (1998)[19]	Multicentric study	8 weeks	699	2 weeks washout phase with nonmedicated emollient and following treatment for 8 weeks 1) Calcipotriol cream 50ug/g in morning and vehicle cream in evening **(group 1)** 2) Calcipotriol cream 50ug/g BD **(group 2)** 3) Calcipotriol cream 50ug/g in morning and Clobetasone 17 butyrate cream 0.5mg/g in evening **(group 3)** 4) Calcipotriol cream 50ug/g in morning and	Patients 18 years and above with psoriasis vulgaris on trunk and or limbs	Most frequent adverse event was skin irritation of face, treated lesions and peri lesional skin and was found to be significantly different between 4 treatment groups. Group 1- 31.2% Group 2- 34.3% Group 3- 23.8% Group 4- 17.1% Group 2 cause most skin irritation Group 3 and 4 cause significantly less irritation.	1.The mean change in PASI score, calcipotriol/vehicle was less effective (p-0.002) than three treatment groups. The mean % change in PASI score shows that 1.calcipotriol/ calcipotriol is as effective as Calcipotriol/clobetasone. 2.Calcipotriol/betamethasone is more effective than calcipotriol/ calcipotriol. 3.No difference found between Calcipotriol/clobetasone group and Calcipotriol/betamethasone group. 3. investigator's overall assessment of treatment response Group 1-28.5% Group 2- 40.2% Group 3- 42.5% Group 4- 54% (p-0.20) 4. Patient's overall assessment Group 1-26.6% Group 2- 40.1% Group 3- 40.1% Group 4- 51.2% (0.04)

©2024Int. J. LifeSci.Biotechnol.Pharma.Res.

DOI: 10.69605/ijlbpr_13.9.2024.44

				betamethasone 17 valerate cream 1mg/gm in evening. **(group 4)**			
Koo et al (2006) [17]	United States	Part 1- 2 weeks Part 2- 24 weeks	86	**Part 1** Clobetasol foam and calcipotriene ointment BD **(group 1-44),** Clobetasol foam BD **(group 2-21),** calcipotriene ointment BD **(group 3-21)** eachfor 2 weeks. **Part 2** Patients in **group 1** who achieved remission ≥50% improvement in target lesion scores (received calcipotriene ointment on weekdays and clobetasol foam on weekends BD for 24 weeks **(group 4-19)** calcipotriene ointment on weekdays and vehicle foam on weekends BD for 24 weeks**(group5-19)**	Patients above 18 years of age with mild to moderate Plaque psoriasis	No adverse events mentioned	**Part 1** 1. Mean overall combined score was significantly lower in group 1 as compared to group 2 (p-0.0017, p-0<0.001) and group 3 (p-<0.0001,p - <0.0001). 2. Mean % reduction in trunk lesion scores- at 2 week was 69.3%, 48.1%, 36.6% in group 1,2,3 respectively. (p-0.0005, 0.0001) 3.Mean % reduction in extremity lesion scores- at 2 week was 70.1%, 40.5%, 31.1% in group 1,2,3 respectively. 4.Investigator global Severity assessment of psoriasis also favoured group 1 as compared to group 2 (p-.0.0080) and group 3 (p-0.0001) 5. Subject Severity Assessment of Psoriasis also favoured group 1 as compared to group 2 (p-.0.2315) and group 3 (p-0.0073) **Part2-** 1.Group 4 maintained greater remission compared to group 5 in both per protocol as well as intention to treat analysis 2. There was no statistically significant difference for all assessment in two groups.
Thakur et al (2018)[1]	India	20 weeks	36	Wash out period of 4 weeks for	Patients between 18 to 70	1.30.30% of patients had hyper	1.Mean modified Palmo plantar psoriasis area Severity index

©2024Int. J. LifeSci.Biotechnol.Pharma.Res.

DOI: 10.69605/ijlbpr_13.9.2024.44

6				topical & 8 weeks for systematic treatment followed by following treatment. Excimer lamp twice weekly on one side **(group 1)** and Calcipotriol (0.005%) Clobetasol propionate (0.05%) combination OD for 12 weeks **(group 2)** followed by follow up after 8 weeks	years of age with moderate to severe Palmoplantar Psoriasis of duration more than 6 months	pigmentation and 3.03% severe photosensitive reaction in group 1 and Atrophy in 9.09% patients in group 2. 2.Adverse effects were significantly more common in group 1 as compared to group 2. 3. There were no side effects observed in either group at 20th week.	(mPPPASI) reduced significantly in group 1 from 7.75 ± 4.62 to 4.01 ± 4.07 (p-<0.001) at 12th week and 2.66 ± 3.97 at 20th week. 2.Mean modified Palmo plantar psoriasis area Severity index (mPPPASI) reduced significantly in group 2 from 7.36 ± 4.46 to 3.55 ± 3.77 (p-<0.001) at 12th week and 2.70 ± 3.97 at 20th week. 3. No statistically significant difference was found between two modalities. 4. Minimal, mild, moderate and marked improvement was seen in 15.2%, 18.2%, 36.4%, and 24.2% respectively in group 1. 5. Minimal, mild, moderate and marked improvement was seen in 3%, 24.2%, 39.4%, and 24.2% respectively in group 2.

Efficacy evaluation (table 1)

The included studies reported comparison of combination of clobetasol and Vit D analogue like calcipotriol, calcipotriene with only vit D analogue or vitamin D analogue / vehicle or vitamin D analogue / betamethasone or only clobetasol propionate. Study done by Thakur et al also compared combination therapy with excimer lamp (MEL).[16]All studies reported use of clobetasol and Vit D analogue like calcipotriol, calcipotriene either concurrently or sequentially for comparison with varied duration from 8 weeks to 26 weeks.

Two studies evaluated mean change in percentage of PASI score and two studies evaluated global severity assessment of psoriasis, overall severity score every 2 weeks. In study by Koo et al, overall severity score at week 2 was significantly lower for combination therapy group as compared to either monotherapy groups. (p=0.0017, p<0.0001) and Global severity assessment of psoriasis showed improvement significantly in combination group as compared to monotherapy groups. (p=0.0001, p=0.0080).[17]In study by Austad et al, after 2 weeks treatment with clobetasol propionate and 4 weeks treatment with calcipotriol showed significantly lower overall severity score. (p < 0.0001)than 6 weeks continuous treatment with calcipotriol.[18]Only in study done by Kragballe, as per mean change in PASI score, combination is more effective as compared to calcipotriol/vehicle group. (p=0.02) and investigator overall assessment of treatment response showed improvement in combination group but was not statistically significant. (p=0.20)[19] In study done by Thakur et al, both the treatment modalities like excimer and calcipotriol-clobetasol combination showed significant reduction in MPPPASI score but the adverse effects were significantly more common in excimer treated patients.(0.002)

Study done by Austad et al also evaluated physician's global assessment of treatment and favoured combination therapy over monotherapy.

All studies reported adverse events like skin irritation, reddish discoloration, pruritis, atrophy with medications and hyperpigmentation, severe photosensitive reaction with excimer lamp.

Psoriasis is a life- long immune mediated inflammatory disease.[12]It is associated with comorbidities such as metabolic syndrome, cardiovascular disease, renal disease, stroke, uveitis and hyperlipidemia. Chronic inflammation links psoriasis with the associated comorbidities. Obesity,lack of sleep, smoking, alcohol and sedentary lifestyle have been associated with worsening of psoriasis. It thus requires a holistic and multi - disciplinary care approach. Lifestyle modifications such as exercise,weight reduction, smoking

©2024Int. J. LifeSci.Biotechnol.Pharma.Res.

DOI: 10.69605/ijlbpr_13.9.2024.44

cessationand abstinence from alcohol help in treating psoriasis.[20]

Clobetasol Propionate in psoriasis

Reygagne et alconducted a multicenter randomized investigator masked parallel group study in patients with moderate to severe scalp psoriasis.Subjects received either clobetasol propionate shampoo 0.05% or calcipotriol solution 0.005%.It was found that the global severity score and total severity score improved in both groups during study with a greater improvement in clobetasol propionate group.[10]

Vitamin D Analogues in psoriasis

Calcipotriene twice daily is safe and effective treatment for plaque psoriasis according to Cochrane systematic review. It is also found to be effective in scalp psoriasis.It is more efficacious than other Vitamin D analogues(tacalcitiol and calcitriol),short contact diathranol and 15% coal tar.Calcitriol has found to be safe and effective in multicenter randomized clinical trials.Tacalcitol has been found to safe and effective in clinical trials in chronic plaque psoriasis.[13]

Clobetasol propionate with Vitamin D analogues combination in psoriasis

We have several systematic reviews on combination of vitamin D analogue and betamethasone for psoriasis treatment. Though both betamethasone and clobetasol are super potent steroids, no systematic review has been conducted for vitamin D analogues and clobetasol combination for psoriasis. Our systematic review included only randomized controlled trials having higher level of evidence.

Our studies have used calcipotriol cream and clobetasol cream on the same day or clobetasol and calcipotriol sequentially or combination preparation. The comparison is done with calcipotriol alone/clobetasol alone /calcipotriol and vehicle/calcipotriol and betamethasone/excimer lamp.

Kragballe K et al demonstrated that calcipotriol and clobetasol applied sequentially is as effective as calcipotriol alone but less effective than calcipotriol betamethasone applied sequentially. Austad J et al found that sequential treatment of the 2 medicines was superior to calcipotriol alone.[18] The combination treatment was found to be more effective than monotherapy by John Koo et al.[17] The combination therapy and excimer lamp was equally effective in treating psoriasis according to Abhishek Thakur et al.[16]

There were many other studies those excluded from our systematic review also reported that combination therapy was more effective as compared to monotherapy. Menter A et al conducted an open label multicenter study in which participants were instructed to apply clobetasol propionate spray 0.05% each morning and calcitriol ointment 3mcg/g each evening for 28 days.The treatment regimen was efficacious with a significant improvement in overall disease severity score at week 4 of the treatment regimen.[14] In another study 15 patients with nail psoriasiswere treated with colorless nail lacquer containing 8% clobetasol 17 propionate applied at bedtime at weekend and Tacalcitol ointment on weekdays.It was found that the combined treatment was safe and effective for nail psoriasis.[21]

Rigopoulos D et al used calcipotriol cream every night 5 times /week during weekdays and clobetasol propionate cream 2 times per week on weekend nights for 6 months for nail psoriasis. Patients were followed up for further 6 months and advised to use clobetasol propionate only 2 nights per week.The treatment led to greater improvement in the subungual hyperkeratosis as expressed by the patients.[22]

CONCLUSION

Topical application of clobetasol and vitamin D analogue is more effective in combination as compared to monotherapy with mild adverse events. As psoriasis is a chronic disease with flare ups and remissions, studies with longer duration using combination need to be carried out. The studies in included in review also lacked uniformity in treatment protocols and outcome measurements. Randomized controlled trials which overcome these limitations need to be carried out and included in future review.

Acknowledgements: We would like to thank Dr. Shilpa Pratinidhi, Dean of Medical College and Dr. Jyoti Landge, Professor and head of department of Community Medicine for their support and guidance.

Funding: Nil

Conflict of interest: There is no conflict of interest

REFERENCES

1. Mysore V, Sacchidanand S, Rao K. Dermatological Diseases: A Practical Approach. 2nd ed. Devi V, Devi K, editors. New Delhi: Wolters Kluver (India); 2016. 50–50 p.
2. Dogra S, Yadav S. Psoriasis in India: Prevalence and pattern. Vol. 76, Indian Journal of Dermatology, Venereology and Leprology. 2010. p. 595–601.
3. Segaert S, Shear NH, Chiricozzi A, Thaçi D, Carrascosa JM, Young H, et al. Optimizing Anti-Inflammatory and Immunomodulatory Effects of Corticosteroid and Vitamin D Analogue Fixed-Dose Combination Therapy. Vol. 7, Dermatology and Therapy. Springer Healthcare; 2017. p. 265–79.
4. Gupta L, D'souza P, Martin A. IADVL's Concise Textbook of Dermatology. 2nd ed. Gupta L, D'souza P, Martin A, editors. New Delhi: Jaypee Brothers Medical Publishers; 2019. 214–214 p.
5. Zhu B, Jing M, Yu Q, Ge X, Yuan F, Shi L. Treatments in psoriasis: from standard pharmacotherapy to nanotechnology therapy. Vol. 39, PostepyDermatologiiiAlergologii. Termedia Publishing House Ltd.; 2022. p. 460–71.
6. Elmets CA, Korman NJ, Prater EF, Wong EB, Rupani RN, Kivelevitch D, et al. Joint AAD–NPF Guidelines of care for the management and treatment of psoriasis with topical therapy and alternative medicine

©2024Int. J. LifeSci.Biotechnol.Pharma.Res.

DOI: 10.69605/ijlbpr_13.9.2024.44

modalities for psoriasis severity measures. J Am Acad Dermatol. 2021 Feb 1;84(2):432–70.
7. Ren J, Zhu Q, Wang S, Li X, Sun Z, Li N, et al. Clinical efficacy and safety of using calcipotriol–betamethasone compounding agent for psoriasis treatment: a systematic review and meta-analysis. Vol. 314, Archives of Dermatological Research. Springer Science and Business Media Deutschland GmbH; 2022. p. 633–41.
8. Rosso JQ Del, Rosso D. Topical Corticosteroid Therapy for Psoriasis-A Review of Clobetasol Propionate 0.025% Cream and the Clinical Relevance of Penetration Modification. Vol. 13, J Clin Aesthet Dermatol. 2020.
9. Nair AB, Kumar S, Dalal P, Nagpal C, Dalal S, Rao R, et al. Novel Dermal Delivery Cargos of Clobetasol Propionate: An Update. Vol. 14, Pharmaceutics. MDPI; 2022.
10. Reygagne P, Mrowietz U, Decroix J, De Waard-Van Der Spek FB, Acebes LO, Figueiredo A, et al. Clobetasol propionate shampoo 0.05% and calcipotriol solution 0.005%: A randomized comparison of efficacy and safety in subjects with scalp psoriasis. Journal of Dermatological Treatment. 2005 Feb;16(1):31–6.
11. Rosso James, Kim Grace. The Rationale Behind Topical Vitamin D Analogs in the Treatment of Psoriasis Where Does Topical Calcitriol Fit In? J Clin Aesthet Dermatol. 2010;3(8):46–53.
12. Raharja A, Mahil SK, Barker JN. Psoriasis: A brief overview. Vol. 21, Clinical Medicine, Journal of the Royal College of Physicians of London. Royal College of Physicians; 2021. p. 170–3.
13. Torsekar R, Gautam M. Topical therapies in psoriasis. Indian Dermatol Online J. 2017;8(4):235.
14. Menter A, Sofen H, Smith S, Papp K, Kempers S, Hudson CP, et al. An Open-Label, Multicenter Study of the Efficacy and Safety of an AM/PM Treatment Regimen With Clobetasol Propionate Spray 0.05% and Calcitriol Ointment 3 μg/g in the Management of Plaque Psoriasis CUTIS Do Not Copy. Vol. 88, Cutis. 2011.
15. Barrea L, Savanelli MC, Di Somma C, Napolitano M, Megna M, Colao A, et al. Vitamin D and its role in psoriasis: An overview of the dermatologist and nutritionist. Vol. 18, Reviews in Endocrine and Metabolic Disorders. Springer New York LLC; 2017. p. 195–205.
16. Thakur A, Bishnoi A, Dogra S, Narang T. Comparison of effectiveness and safety of excimer lamp vs topical calcipotriol-clobetasol propionate combination in the treatment of palmoplantar psoriasis. PhotodermatolPhotoimmunolPhotomed. 2018 Jul 1;34(4):249–56.
17. Koo J, Blum RR, Lebwohl M. A randomized, multicenter study of calcipotriene ointment and clobetasol propionate foam in the sequential treatment of localized plaque-type psoriasis: Short- and long-term outcomes. J Am Acad Dermatol. 2006 Oct;55(4):637–41.
18. Austad J, Bjerke JR, Gjertsen BT, Helland S, Livden JK, Morken T, et al. Clobetasol propionate followed by calcipotriol is superior to calcipotriol alone in topical treatment of psoriasis. 1998.
19. Kragballe K, Barnes L, Hamberg KJ, Hutchinson P, Murphy F, Møller S, et al. Calcipotriol cream with or without concurrent topical corticosteroid in psoriasis: tolerability and efficacy on behalf of 53 centres from six countries. Vol. 139, British Journal of Dermatology. 1998.
20. Ko SH, Chi CC, Yeh ML, Wang SH, Tsai YS, Hsu MY. Lifestyle changes for treating psoriasis. Vol. 2019, Cochrane Database of Systematic Reviews. John Wiley and Sons Ltd; 2019.
21. Regana MS, Balbas GM, Millet PU. Nail psoriasis: A combined treatment with 8% clobetasol nail lacquer and tacalcitol ointment. Journal of the European Academy of Dermatology and Venereology. 2008 Aug;22(8):963–9.
22. Rigopoulos1 D, Ioannides2 D, Prastitis1 N, Katsambas1 A. Nail Psoriasis: A Combined Treatment Using Calcipotriol Cream and Clobetasol Propionate Cream.

©2024Int. J. LifeSci.Biotechnol.Pharma.Res.