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Efficacy and Safety of Calcipotriol / Betamethasone Dipropionate Topical Gel Used to Psoriasis Treatment

Komal Machhindranath Halwar[1], Khushbu Sanjay Pawar[2], Harshada Gajanan Kamalkar[3]
Monika Dnyaneshwar Dange[4], Prof. manisha Ramesh Virkar[5], Dr. Kavita Kulkarni[6]
Students[1,2,3,4]
Guide, M. Pharm Pharmaceutics[5]
Principal, PhD. M Pharm[6]
Department of Quality Assurance
Gajanan Maharaj College of Pharmacy Chh. Sambhajinagar, Maharashtra, India

Abstract: *Psoriasis is the one of the most common skin disease. According to the reasearch Psoriasis disease is widely show in human at recent now, this is a long term disease it is triggered by the genetic issue, bad habit such as smoking, drinking, drug addiction etc. and some long term medication, insect bite etc. it can be affecting adult, child or old age people also. Now days latest research we have lot of option in drug or dosage form. In the topical dosage form GEL dosage form is the best option because of their application or improves patient compliance. It is big option for those drugs who had a problem with solubility with the*

dosage form. In the gel any drug can be easily incorporated. GEL can be easily applied or removed form skin by the single wash, their no extra afford need to rubbed on skin as compare other dosage form only just make single thin layer of skin. It also the problem with children dosing. Drug can be shows better effect on penetration on skin, and also increase bioavailability of drug. There is no adverse effect or using humectant cool the skin and relief form pain and itchy dry skin. While topical medications remain the cornerstone of the psoriasis treatment paradigm, they also come with the risk of multiple side effects. An alternative topical treatment option, calcipotriene or calcipotriol, is a vitamin D derivative that is thought to work by inhibiting keratinocyte proliferation and enhancing keratinocyte differentiation. Multiple studies have demonstrated its efficacy and safety in improving psoriasis when used in combination with topical corticosteroids. Given the effectiveness and side effect profile seen with this combination of topical steroid and calcipotriene, the US Food and Drug Administration approved a calcipotriene/ betamethasone dipropionate product for use in psoriasis patients over the age of 12 in 2006. Our paper seeks to review clinical trial evidence of this combination medication and its use in the treatment of psoriasis vulgaris. While assessment of available evidence indicates that the topical medication is both safe and effective for the treatment of psoriasis vulgaris, addressing limitations of what is known, such as tolerability, adherence, and patient preference, of this combination drug in future high-impact studies is needed.

Combination topical corticosteroids and vitamin D analog treatments for nail psoriasis are widely used in cream and ointment vehicles, but patients may prefer a foam vehicle due to ease of application and favorable cosmetic appearance. Calcipotriene 0.005%/betamethasone dipropionate 0.064% (Cal/BD) aerosol foam is an FDA approved therapy for plaque psoriasis, but may also be an effective treatment for nail psoriasis in a novel aerosol foam.

Keywords: calcipotriene, betamethasone diproprionate, psoriasis, topical treatment, steroids, Vitamin D.

I. INTRODUCTION

Psoriasis is a lifelong, chronic, and immune-mediated systemic disease with preferential skin involvement, which affects approximately 1–3% of the Caucasian population . Psoriasis may appear at any age; however, over 75% of

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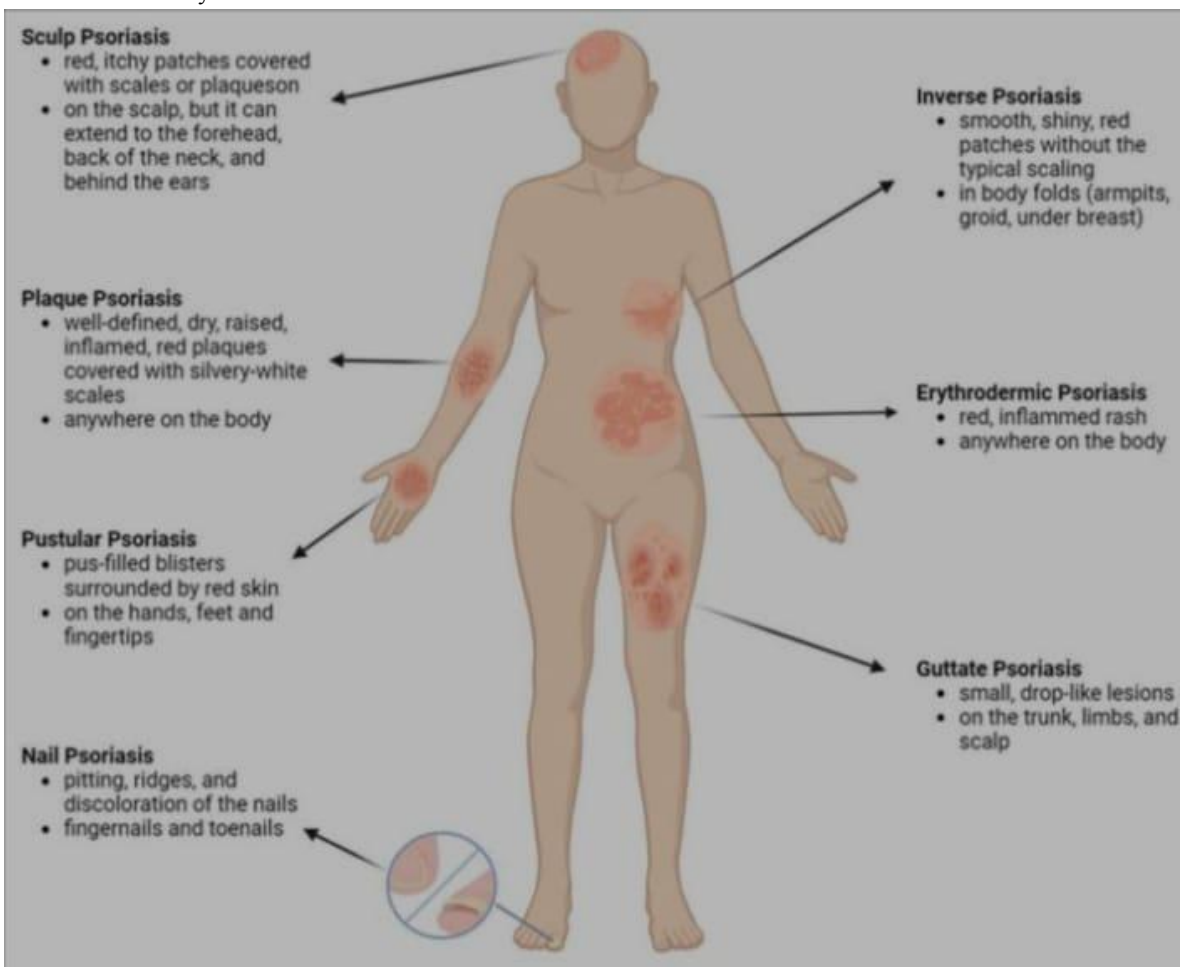
patients belong to a clear subgroup, that develops t**he** disease before the age of 40 (type 1 or early-onset psoriasis) .The most common clinical variant is plaque-type psoriasis, characterized by erythematous scaly plaques, round or oval, variable in size, frequently located in scalp, lower back, umbilical region, intergluteal cleft, knees, and elbows . As a clinically heterogeneous disease, psoriasis presents several degrees of severity and a wide array of presentations in different patients . Approximately 80% of psoriasis patients have mild disease, with skin plaques usually covering less than 10% of the body surface area (BSA). However, some patients have moderate to/or severe disease, with greater than 10% of the BSA involvement . The different presentations of psoriasis require a variable approach to treatment and the current treatment concept advocates that the type of therapy prescribed should be appropriated to disease severity. Although there is a wide range of therapies available for the treatment of psoriasis, either systemic or topical agents, the use of topical therapy (Figure 1) remains a key component of the management of almost all psoriasis patients. While mild disease is commonly treated only with topical agents, the use of topical therapy as adjuvant therapy in moderate-to-severe disease may also be helpful and can potentially reduce the amount of phototherapy or systemic agent required to achieve satisfactory disease control.



Preparation:

Preparations containing calcipotriol combined with betamethasone (in the form of betamethasone dipropionate) are available for the topical treatment of mild psoriasis [1,2]. The topical formulations of calcipotriol with betamethasone available in most countries are ointments, gels, and foams [3–6]. The specific properties of the these preparations may not be comprehensible to every clinical practitioner. The aim of this article is to review the similarities and differences between these three formulations. In this article, we use the terms "foam" and "foam containing calcipotriol with

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betamethasone" interchangeably as equivalent to "foam containing calcipotriol with betamethasone dipropionate", the terms "ointment" and "ointment containing calcipotriol with betamethasone" as equivalent to "ointment containing calcipotriol with betamethasone dipropionate", and the terms "gel" or "gel containing calcipotriol with betamethasone" as equivalent to "gel containing calcipotriol with betamethasone dipropionate.

ADVANTAGE

Calcipotriol can be reduce redness, swelling and itching.
Slow skin cell growth

II. METHOD

A total of 50 patients were recruited for a national, multicenter, randomized, open controlled trial from nine centre. Patients aged >18 years were included in the study if they bad mild-to-moderate plaque psoriasis. The main exclusion criteria were: severe forms of plaque-type psoriasis, guttate erythrodermic and pustular psoriasis, cutaneous atrophy, and suspended abnormality in calcium homeostasis. Patients who were treated with systemic therapies or phototherapy within the previous 4 weeks or with any topical treatments during the last 2 weeks were excluded. Ia addition, women who were pregnant or breast feeding were also excluded. The study was approved by all local ethics committees. According to a computer-generated randomization schedule, eligible patients who had given written informed consent were assigned to two groups, in a 1:l ratio, to receive: Group A - calcipotriol 5O Pdgl betamethasone dipropionate 0.5 mg/g(Dovobet) topically administered once daily for 4 weeks, followed by maintenance of calcipotriol @aivonex$ 50 pglg 66som, applied twice daily for 8 weeks; sod Group B - calcipotriol (Daivonex) 50 mg/ cream topically administered trice daily for 12 weeks. The treatment allocation was done providing conserve coded drug boxes. Changes in the Psoriasis Area sad Severity Index (PASD (16) after 4 weeks of treatment were considered the primary outcome reassure. Secondary objectives included: (i) maintenance of the PASI score with calcipotriol as a sequential therapy in the following 8 weeks; (D safety of the study drugs; and (iii) patient's' quality of life, as assessed by the Skindex29, which is a validated instrument characterized by three scales scoring essential areas (i.e. burden of symptos social functioning, and emotional state) . Efficacy, safety and quality of drug

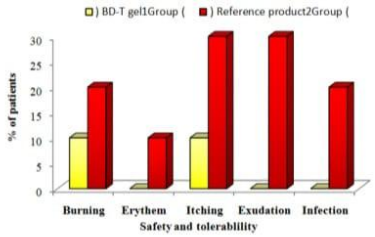

Fig. 4: Comparison between the two groups as regards safety and tolerability

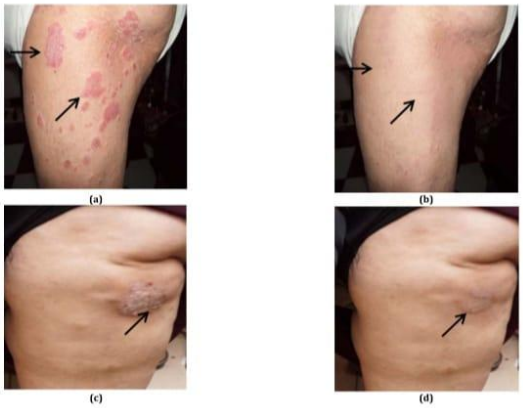

Fig. 5: A female patient with plaque type psoriasis: (a) left leg before treatment (PGA 4), (b) left leg after treatment with BD-T gel, (PGA 1
A female patient with plaque type psoriasis; (c) left leg before treatment (PGA=3) and (d) left leg after treatment with diprosone cream
for 2 mo (PGA=1), PGA is physician global assessment, BD-T gel is betamethasone dipropionatel oaded transfers omalgel

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III. DISSCUSSION

Calcipotriene/betamethasone dipropionate gained FDA approval in 2006 and is indicated for the treatment of psoriasis vulgaris in patients 12 years of age and older. It is a combination product containing a fixed combination of 0.005% calcipotriene hydrate, a synthetic vitamin D3 analog, and 0.064% betamethasone dipropionate, a synthetic corticosteroid, in either a foam, gel/suspension, or ointment formulation. It exerts its action via reducing hyperproliferation and promoting differentiation of keratinocytes, with the added benefit of steroidal immunoregulatory and anti_inflammatory effects. The recommended use of calcipotriene/betamethasone dipropionate is topical application to affected areas of the body once daily for up to 4 weeks. Application should be discontinued when psoriasis control is achieved. Per its prescribing information, it should be applied to no more than 30% of total body surface area or to use with occlusive dressings. The two Compound product should not be applied to the face, axillae, groin, or thin skin areas and is contraindicated in patients with a history of hypersensitivity to any of the components, patients with disorders of calcium metabolism, and patients with erythrodermic, exfoliative, and pustular psoriasis. For patients ages 12–17 years, and patients 18 years and older, it is recommended not to exceed use of 60 g and 100 g per week, respectively. During the course of treatment, patients should be monitored for adverse drug effects, similar to corticosteroid monotherapy. Calcipotriene/betamethasone dipropionate is a pregnancy Category C drug, with no clinical studies examining its excretion in breast milk.39,40 Topical therapies are primarily used in the management of mild-to-moderate psoriasis; however, they are also employed as adjuvant therapy for resistant lesions or more extensive disease when used concomitantly with phototherapy or systemic agents.41 Systemic agents are generally more expensive and more difficult to use over the long-term, with larger and generally more severe side effect profiles. Topical therapies typically have a more tolerable side effect profile with low systemic absorption; however, they often have vigorous regimens that are difficult for patients to maintain. Calcipotriene/betamethasone dipropionate is recommended for once-daily use, making it a practical option for patients, which simplifies the treatment regimen and improves patient compliance. This single-agent combination drug has been examined extensively during the last several years, with studies demonstrating that once-daily topical application of the combination calcipotriene/betamethasone dipropionate is more effective than monotherapy with either component in patients with psoriasis vulgaris. The clinical trials included in this review are larger, well-designed, randomized, and nonrandomized double-blinded control trials with moderate-to-high-quality evidence. All clinical trials showed a high degree of consistency in the efficacy of the combination drug with statistically significant reduction in PASI or greater percentage of patients cleared of the disease. Different formulations of calcipotriene/betamethasone dipropionate are more efficacious in controlling disease than either monotherapy or vehicle control, which is in agreement with previous studies investigating optimization of treatment and vehicle preparation. The combination of both calcipotriene and betamethasone may also have a positive effect on increased adherence for patients with psoriasis, who often use a variety of medications as part of their treatment plan. Poor adherence to treatment plans may occur for a variety of reasons, one of which is a complicated regimen with multiple steps and multiple medications.44 The more complex a treatment plan, the more time intensive and financially intensive it is, making adherence for patients increasingly difficult. The single-agent combination of topical steroid with vitamin D derivative has the advantage of improving adherence by allowing for only topical application of one medication rather than two. Furthermore, inconvenience, frustration with medication efficacy, as well as fear of side effects are also reasons cited by patients who do not follow their psoriasis treatment plans.44–46 These reasons for nonadherence can be minimized through the use of the calcipotriene/betamethasone combination, as it reduces medication application time and may reduce fears about steroid side effects. Steroid phobia occurs with topical corticosteroids when patients are fearful of using these medications and discontinue treatment. The use of the combination medication may help reduce these fears as it provides a topical medication that is safe for daily use and does not consist wholly of topical steroid. In addition to better adherence, another potential advantage of the combination drug is that it minimizes the unpredictability that accompanies the use of two separate topical medications, which could effectively change the vehicle and lead to unpredictable effects on absorption. Calcipotriene/betamethasone dipropionate should be considered an initial therapeutic modality for psoriasis vulgaris as it is consistently effective and well tolerated.

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Efficacy:

By the end of treatment, 50 patients (85%) demonstrated treatment success according to IGA ; 13 of these patients had clear disease (IGA) at week 4 and left the trial per protocol. By week 2, treatment success was reported in 37 patients (47%) by IGA. There was an 80% improvement in the mean TSS from 71 at baseline to 14 at the end of treatment (Fig. 4). Of note, a 63% improvement in mean TSS was already observed at week 2. The incidence of treatment success according to TSS also increased over time and was achieved by 40 patients (63%) by the end of treatment. With respect to PaGA, the number of patients reporting treatment success increased over time, reaching a total of 45 patients (87%) at the end of treatment (Fig. 3). Similarly to the inves- tigator assessment, 26 patients (56%) had achieved treatment success by week 2. Patients also reported pruritus relief during the study, and by the end of treatment 50 patients (96%) reported no or mild pruritus.

Safety:

Safety and tolerability Adverse events Twenty-seven patients (35%) reported 64 AEs. Most of the AEs were mild (33 of 64) or moderate (22 of 64) in severity, with nine reported as severe. No serious AEs were reported. The AEs reported in most patients were headache (n = 4, 5%), pharyngitis (n = 4, 5%), upper respiratory tract infection (n = 4, 5%) and decreased urine calcium (n = 3, 4%). Two patients (3%) reported a lesional/perilesional AE on the scalp: alopecia (mild, not related to study treatment as considered by the investigator) and application-site pruritus (mild, probably related). One patient experienced unacceptable AEs (not related to study treatment as considered by the investigator), including urine calcium decrease, blood parathyroid hormone increase and urine phosphorus decrease, as the primary reason for withdrawal from the trial. Seven adverse drug reactions (AEs for which a causal relationship with the study drug was possible or probable according to the investigator) were reported in five patients as single events. Three of these events occurred in one patient: blood calcium decrease, blood parathyroid hormone increase and urine calcium decrease (notably, these events occurred in a separate patient from the aforementioned ‘unacceptable AEs’). The others all occurred individually (Table 2); blood parathyroid hormone increase, urine calcium decrease and acne were moderate in severity, and all other adverse drug reactions were mild. A mild acneiform rash (dermatitis acneiform) occurred at week 4 on the face of a female patient aged 16 years, with an 8-year history of psoriasis, who was treated concomitantly with hydrocortisone cream for flexural psoriasis behind the ears. The acneiform rash was not treated and was still ongoing 2 weeks after the last on-treatment visit. A headache was

IV. CONCLUSION

Calcipotriol/betamethasone foams show significantly higher efficacy compared to ointment and gel formulations in the treatment of plaque psoriasis. The higher clinical efficacy may be attributed to the supersaturation technique which was used for the production of the foam formulations. Gels and ointments have shown some benefits in the topical treatment of scalp and nail psoriasis, respectively. The available data indicate that the foam formulation may close the gap between topical and systemic therapy in plaque psoriasis, particularly when applied as a long-term proactive maintenance treatment.

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[2]. Department of Dermatology, D. Y. Patil School of Medicine, Navi Mumbai, Maharashtra, India

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[11]. BM College of Pharmaceutical Education and Research Indore, M.P (India)