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A COMPREHENSIVE REVIEW ON CLOBETASOL PROPIONATE CREAM

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❖ ABSTRACT:

Topical corticosteroids are the most often prescribed medications for treating a range of dermatoses (TC). Because of their potent symptom-relieving effects, these drugs are licensed for the treatment of inflammatory and pruritic symptoms of dermatologic illnesses. The most commonly used topical medication (TC) to treat skin diseases is clobetasol propionate (CP), which reduces oedema, redness, and irritation. Topical corticosteroids have vasoconstrictive, anti-inflammatory, and anti-pruritic properties. Clobetasol propionate inhibits the synthesis of inflammatory mediators and produces anti-inflammatory proteins by binding to cytoplasmic glucocorticoid receptors and activating glucocorticoid receptor-mediated gene expression. This case series discusses the efficacy, safety, and clinical experience of using CP 0.025% topical therapy to treat a variety of dermatologic conditions.[1]

❖ **Keywords:** Clobetasol, Cream, Dermatoses

❖ INTRODUCTION:

The treatment of many different dermatological conditions is greatly aided by topical corticosteroids (TC). Owing to the wide range of TC-based formulations and their superior efficacy, they are utilized for treating various disease stages and anatomical sites.One The most common type of psoriasis, plaque-psoriasis, involves 85–90% of individuals and is characterized by raised plaques that are red, well-defined, oval or irregularly shaped, and covered in silvery scales. Treatment for moderate-to-severe clinical signs and symptoms of plaque psoriasis involves using clobetasol propionate (CP) 0.025% cream.

The strongest topical steroid that is authorized for application is CP.It contains anti-inflammatory, immunosuppressive, and antimitotic properties in addition to inhibiting the synthesis of cytokines. It also modifies the distinct cells' development, differentiation, and functions.

The 0.025% cream formulation of CP does not contain propylene glycol, short-chain alcohols (such as ethanol), or sorbitan sesquioleate, an emulsifier based on sorbitol that is frequently an allergy in many TC formulations. For those 18 years of age and older, CP is a topical TC treatment applied twice daily to treat moderate-to-severe plaque psoriasis. CP 0.025% becomes much more effective when pharmaceutical-grade diethylene glycol monoethyl ether is added.

These case studies explore the efficacy, safety, and experience of using CP 0.025% to treat a variety of dermatological condition

❖ Physicochemical Properties and Metabolism of Clobetasol Propionate

With a solubility of 2 µg/mL in water, clobetasol-17-propionate is a crystalline powder with a white to cream appearance and no smell. This moiety's chemical structure is displayed in Figure 1. It has the same molecular weight as prednisolone (466.97 g/mol), a melting point of 196.25 °C, and a log P value of 2.98. Its chemical name is [(8S,9R,10S,11S,13S,14S,16S,17R)-17-(2-chloroacetyl)-9-fluoro-11-hydroxy-10,13,16-trime-thyl-3-oxo-6,7,8,11,12,14,15,16-octahydrocyclopenta[a] phenanthren-17-yl] propanoate, with the empirical formula C25H32ClFO5.

At λ_{max} 237 nm (in methanol), CP exhibits distinctive UV absorption. From a photochemical perspective, this particular molecule is highly attention-grabbing due to its two spatially split chromophores: the cyclohexadiene moiety in ring A and the carbonyl group at C-20.

Through the removal of 4, 5 double bonds, the hydroxylation of the 3-keto group, and the reduction of 20-keto to 20-hydroxy form, hepatic microsomal enzymes metabolize corticosteroids. The metabolites aremoreover conjugated with glucuronic or sulfate acid and eliminated in the urine. There is hardly any systemic absorption of CP after cutaneous application.[55]

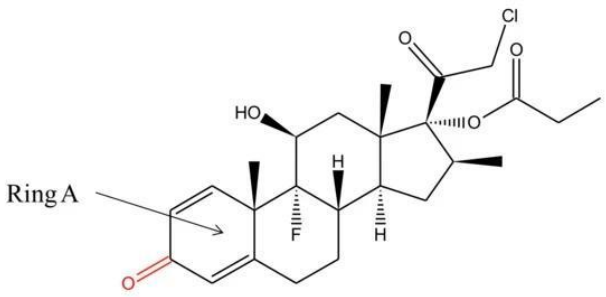

Figure 1.Chemical structure of clobetasol propionate

❖ Mechanism of Action of Clobetasol Propionate

In most cases, CP is given to treat and control conditions including psoriasis, granulomatous diseases, discoid lumps erythema, dry hyperkeratotic dermatoses, eczema, and atopic dermatitis.Two distinct pathways (nongenomic and genomic) are followed by corticosteroids at the cellular level. The glucocorticoid receptors (GR) in the genomic route are activated by cortisol, which also causes receptor homodimerization and binding to GREs (glucocorticoid-responsive elements). Figure 2 shows the CP's mechanism of action.

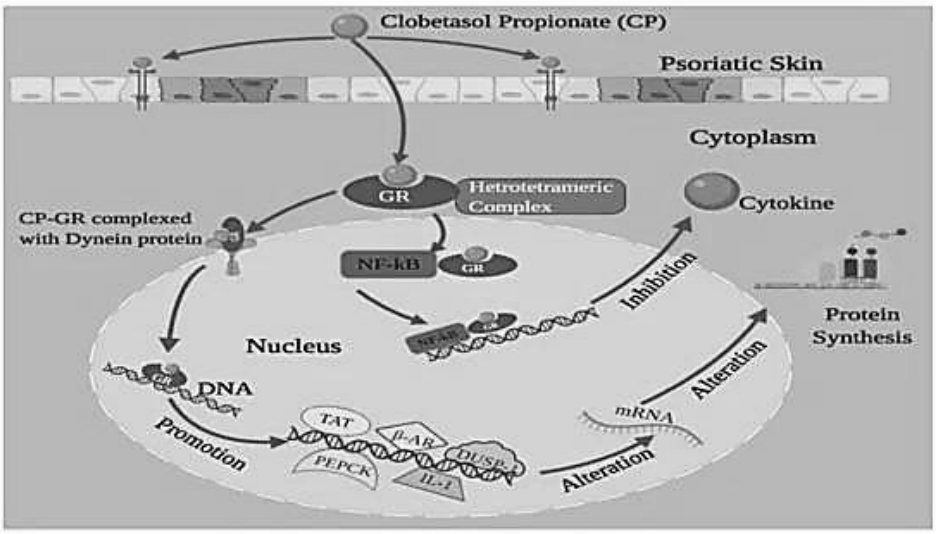

Figure 3. Mechanism of action of clobetasol propionate after topical application. GR—GlucocortiCoid Receptor; TAT—tyrosine aminotransferase; PEPCK—phosphoenolpyruvate carboxykinase; β-AR—beta-adrenergic receptor; DUSP—dual-specificity protein phosphate; NF-κb—nuclear factorKappa-light-chain-enhancer;IL-1—interleukin 1; mRNA—messenger RNA.

The early therapeutic benefit of glucocorticoids is due to the nongenomic pathway. Particular attention is given to membrane-bound receptors and second messengers in this route. It is not necessary to produce new proteins for this course to work; instead, it modifies the activation levels and response of the target cells (monocytes, platelets, and T cells) .

Initially attaching to the steroid-binding site of intercellular GR, glucocorticoids then translocate to the nucleus where they finally modify the transcription of the gene. Intracellular GR is attached to heat-shock protein 90 (Hsp90) and immunophilin (stabilizing proteins) in an unbound (steroid-free) state. The transcription of genes cannot be influenced by the receptor in its steroid-free, or unbound, form. An interchange of chaperone proteins results from a conformational change triggered by steroid binding. These proteins enable the dynein protein trafficking pathway to bind with the steroid-GR complex, which translocates the steroid the nucleus through the cytoplasmic oid-GR complex. Following the transcription of genes via GR dimerization, palin-dromic promoter sequence binding, and GREs, anti-inflammatory functions (phosphoenol pyruvate carboxykinase (PEPCK), dual-specificity protein phosphatase 1 (DUSP-1), tyrosine aminotransferase (TAT), β-adrenergic receptor, IL-10, and IL-1-receptor antagonist) are promoted. The binding of the glucocorticoid-GR dimer either represses or stimulates the transcription of genes that are sensitive, resulting in variations in the synthesis of mRNA and thereafter changes in the synthesis of proteins.

Corticosteroids not only directly control gene transcription but also indirectly control transcription by blocking other transcription factors. Specifically, these moieties have been shown to stimulate the expression of the IkBa gene, which raises the levels of the inhibitory nuclear factor-κBa (IκBa) at the cellular level. By interacting with another transcription regulator, NF-kB (nuclear factor-kB), the IkBa protein, in turn, inhibits transcription by preventing translocation to the nucleus. Since this gene does not have glucocorticoid-susceptible receptors, corticosteroids may have an effect on its transcription. Additionally, corticosteroids have been shown to reduce T lymphocyte proliferation. CP has the ability to prevent the synthesis of arachidonic acid metabolic products. Though it is unclear, these actives may inhibit cytokine expression as well as reduce cytokine effects in their antiproliferative activity [19]. Reportedly, the serum of patients receiving glucocorticoids for inflammatory skin conditions showed decreased levels of leukotrienes, prostaglandins, and arachidonic acid metabolic products.[55]

❖ CLOBETASOL PROPIONATE 0.025% IN THE TREATMENT OF PSORIASIS:

Psoriasis is a skin condition where cells grow at a faster rate than they can be shed, causing excess skin to build up and form scaly patches on the body.It appears to be a build-up of dry skin on your body. You can have it at any age, but normally as you get older. It starts with the skin cracking as a paper cut on your fingertips. This skin would begin to die, flake, peal and itch. As your itch the area, it begins to get red and then it begins to blister, flake and peels to raw skin. It appears most often on hands, toes, the inside arch of your feet and on your heels. It is also shows up in callus, by cracking. When washing hands it has a burning effect.

Living in moist humid climate appears to delay the condition for appearing. Dry arid climates seem to aggravate the condition. Washing your hands has a drying affect, which triggers the condition. When washing, water removes oils from our body, and has a drying effect on our hands. Washing with Psoriasis removes the dry skin, but then the skin underneath is raw. Hard water appears to worsen the condition in dry climates, but not as much in humid areas. Soft water appears better.

About 0.44–2.8% of adults in India suffer from psoriasis, a persistent inflammatory skin condition [2,3]. Psoriasis is a substantial global burden that has a significant detrimental impact on patients' quality of life, with prevalence rates ranging from 0.09 to 11.43% across nations [4]. Anywhere on the body, psoriasis symptoms can appear. They are typically characterized by erythematous, scaly plaques that are persistent, well-defined, and unpleasant. While rarely life-threatening, these enduring symptoms have an impact on social, psychological, and physical functioning and continue to be extremely difficult for patients with illness sequelae to manage [5,6].

Topical treatments including corticosteroids and vitamin D3 analogs are typically advised for the majority of patients with mild [Psoriasis Area Severity Index (PASI) B 10] to moderate (PASI[10 but B 20]) psoriasis [7, 8, 9]. For severe psoriasis, systemic treatments such as phototherapy, acitretin, methotrexate, cyclosporine, or biologic therapy are advised. On the other hand, topical therapies are used as an adjuvant treatment for patients receiving systemic or phototherapies, depending on the severity of their psoriasis, body location, lesion thickness, degree of erythema, and quantity of scaling [5, 9, 10]. For patients with moderate-to-severe psoriasis, topical corticosteroids are the most often given therapy, and there are currently a number of various kinds of formulations available [11] Psoriasis has been shown to cure quickly and effectively with clobetasol propionate, an ultra-high potency (super strong) topical corticosteroid when compared to other corticosteroids [12–13].

Even at the suggested dosage of as little as 2 g/day, the extremely high potency of clobetasol propionate 0.05% emollient cream increases systemic absorption, which may increase the risk of systemic adverse effects like hypothalamic-pituitary-adrenal axis (HPA) suppression. Because of this systemic side-effect, patients are typically only prescribed clobetasol propionate 0.05% cream for tiny regions and for a maximum of two weeks at a time [14]. The need to create innovative formulations with clobetasol propionate concentrations of 0.025 percent, which would offer a desirable benefit-risk profile, is therefore unfulfilled. In patients with moderate-to-severe psoriasis, clobetasol propionate 0.025% (Impoyz~) cream treatment resulted in a lower systemic absorption, resulting in a lower incidence of HPA axis suppression, with a better safety profile compared with marketed clobetasol propionate 0.05% (Temovate) cream. This was demonstrated in a recent phase 2, randomized, open-label clinical study conducted in the United States. [15] In Indian patients with moderate-to-severe psoriasis, we sought to assess and contrast the safety, efficacy, and suppression of the HPA axis with two formulations of clobetasol propionate 0.025% cream [formulation 5 (Impoyz) and formulation 13] and the currently marketed clobetasol propionate 0.05% emollient cream (reference formulation).

- **METHODS:**

1. Patients

Adults aged 18 years or older who had a clinical diagnosis of moderate-to-severe psoriasis affecting at least 25% of their body surface area (BSA; this excludes the scalp, face, groin, axillae, and/or other intertriginous areas, if present) were included in the study. A Psoriasis Global Assessment (PGA) score of C 3 at screening and baseline, as well as

the absence of any signs of aberrant HPA axis function [confirmed by an Adrenocorticotropic Hormone (ACTH) test] at screening, were the other inclusion criteria.The trial excluded patients who had a history of psoriasis that did not improve with topical corticosteroid therapy, were hypersensitive to clobetasol propionate, had an adverse pharmacological reaction to cosyntropin injection (adrenocorticitropic hormone), or both. An acute adrenal crisis, Addison's disease, atopic/contact dermatitis, liver disease, renal impairment, heart disease, diabetes, severe respiratory disease, rheumatoid arthritis, malignancies, and immunocompromised conditions were among the other conditions that precluded patients from participating in the program. Pregnant or lactating women were among the other exclusion criteria, as were patients receiving radiation therapy, anti-neoplastic agents, immune suppressants, antipsoriatics, biological therapies, or immunosuppressive medication within 4 weeks of study treatment, 8 weeks of study treatment, or 2 weeks prior to screening to ensure full washout of previously administered medications to prevent drug interactions.

2. Study design

Two formulations of clobetasol propionate 0.025% cream (formulations 5 and 13) and clobetasol propionate 0.05% cream were studied in patients with moderate-to-severe psoriasis in this phase 2a, randomized, multicenter, active-controlled, investigator-blinded, parallel group, 3-arm trial. REF/2018/01/016779 is the registration number for this study. The purpose of the study was to compare the safety, effectiveness, and suppression of the HPA axis of twice-daily use of clobetasol propionate 0.025% formulations (formulations 5 and 13; produced by Dr. Reddy's Laboratories) with the reference formulation (clobetasol propionate 0.05% cream; produced by PharmaDerm). Two weeks of therapy, followed by a 14-day follow-up, preceded the seven-day screening phase of the trial.

For further details, refer to the supplementary material. An Institutional Review Board and Dependent Ethics Committee at each of the six study sites evaluated and approved the informed consent form and study protocol. According to the rules of Good Clinical Practice, the International Council for Harmonization, and the ethical principles outlined in the Declaration of Helsinki, the study was carried out.

The respective Ethics Committees evaluated and approved the informed consent forms before the patients were enrolled in the trial.

3. Study Assessment

According to the ACTH test (B 18 lg/100 ml) on day 28, the proportion of patients with abnormal cortisol levels was the primary safety objective. At days 7, 14, 21, and 28, the secondary safety outcomes were the amount of time to an aberrant cortisol value and the change in indicators of atrophogenicity from baseline. During scheduled visits, the investigator used visual assessment to determine the drug's local cutaneous atrophogenic activity. The study medication's impact was rated from 0 (none) to 3 (pronounced) for atrophy and from 0 (none) to 4 (strong).

spoken in order to describe telangiectasia In addition, records were kept of clinical laboratory investigations, adverse events (AEs), physical examinations, vital signs, and local tolerability—the patient's assessment of burning, stinging, and itching. An 0 (none) to 3 (severe) scale was used to rate the intensity of burning/stinging and pruritus.

PGA's mean score, the proportion of patients with clear or nearly clear skin, and the distribution of PGA scores at each time point were among the secondary efficacy objectives.

The investigator conducted planned visits wherein the disease severity was clinically determined utilizing the PGA scale. A scale of 0 (clear) to 4 (moderate-to-severe) was used to score the PGA using five severity ratings

4. Treatment, Randomization and Blinding

This formulation contained 0.025% clobetasol propionate along with inert ingredients such as mineral oil, sorbitol, butylated hydroxytoluene, diethylene glycol monoethyl ether, lanolin, propyl paraben, butyl alcohol, and cetyl alcohol, as well as purified water Inactive ingredients included in Formulation 5 included butylated hydroxytoluene,

diethylene glycol monoethyl ether, methyl and propyl parabens, white wax, isopropyl myristate, cyclomethicone, and 0.025% clobetasol propionate.

Patients were randomly assigned 1:1:1 to receive either clobetasol propionate 0.05% cream or formulation 5, formulation 13 (using PROC PLAN in SAS, version 9.2). The study investigator designated the target lesion regions (at least 25% BSA), and patients were told to topically administer the study medicine to those locations twice a day for a duration of 28 days. The study's products were applied as fingertip units (* 0.5 g). In order to cover 25% BSA (3.5 g), patients were instructed to apply seven fingertip units.

The study label was used to conceal the commercial labeling of comparison products, thereby blinding the treatments. The treatment code was concealed from the investigator until data-Base lock.

5. Statistical Analysis

Clobetasol propionate 0.025% formulation 5, formulation 13, or clobetasol propionate 0.05% cream were to be randomly assigned (1:1:1) to a total of ninety participants. The per-protocol (PP; all randomized patients who completed the baseline and end-of-treatment visit and who had no major protocol violations) and modified intention-to-treat (mITT; all randomized patients who received study medication and had at least one post-randomization measurement) populations were the two groups in which the effectiveness assessments were examined. In the safety population—all patients who were randomized at baseline and received at least one dose of study medication—safety assessments were carried out.

Statistical evaluation was conducted using the SAS program (SAS Institute Inc., USA, and Version 9.2). A chi-square test (Fisher's exact test) was used to compare the proportion of patients in each group who had clear or nearly clear PGA and abnormal ACTH stimulation at each time point. When comparing two formulations of clobetasol propionate (0.025 formulation 5 vs. clobetasol propionate 0.05% cream and clobetasol propionate (0.025 formulation 13 vs. clobetasol propionate 0.05% cream), the Marascuillo approach was employed.

❖ CLOBETASOL PROPIONATE 0.05% CREAM IN TREATMENT OF CHRONIC HAND ECZEMA

A chronic inflammatory skin condition that affects only the hands, known as chronic hand eczema (CHE), lasts for three months or more, or it recurs two or more times in a year.[16] Rrecurrent or persistent episodes that last for many years are typically a feature of the clinical processes, even though the majority of CHE patients have mild to moderate disease.[17] The two primary causes of CHE are clearly atopic constitution and exposure to atopic chemicals. Many occupational exposures, particularly those in the manufacturing and healthcare sectors, can either develop or worsen chronic ocular hypertension (CHE).[18,19] Nickel sulfate may be a significant allergen that aggravates hand eczema, according to certain research.[20,21] Atopic dermatitis, allergic rhinitis, asthma, and other similar conditions are also present in roughly 1/3 to ½ of patients with CHE, either personally or through family members.[20, 31–32] Atopic dermatitis (AD) is a past condition for individuals with a higher prevalence of CHE in women than in males [22, 23,24] For individuals with CHE, patch testing are therefore typically advised in order to identify potential allergens. The economic cost of CHE is also shown to be high and noteworthy by evidence.[25–26] These days, there are many different therapeutic techniques used to treat CHE. These include radiation, oral or topical corticosteroids, calcineurin inhibitors (tacrolimus, pimecrolimus), oral immunosuppressant (cyclosporin, mycofenolate mofetil, methotrexate),

Phototherapy; barrier cream and gloves; topical or oral retinoids; emollients; antimicrobial agents.[27, 28] Still, it's unique in thatIt's crucial to minimize allergy exposure as soon as you can.

The mainstay of treatment for eczema is topical glucocorticoids.[28] For the treatment of CHE, individuals who refuse glucocorticoids or who become resistant to them may be evaluated for calcineurin inhibitors, such as tacrolimus or pimemox.Studies have indicated that pimecrolimus has fewer side effects than tacrolimus.[29,30]

Oral immunosuppressant's, such as cyclosporine, methotrexate, and azathioprine, can also be used to treat patients with CHE when topical treatment, phototherapy, and oral retinoids are not beneficial. Its effectiveness stems primarily from immunosuppressant's' good results in treating atopic dermatitis.[33,34]

Even if these therapies work well in the short term, there is a significant chance that dermatitis will return once the treatment is stopped. In hospitals, topical corticosteroids have been used extensively. Strong anti-inflammatory and anti-proliferative effects are observed in the topical 0.05% clobetasol cream, which is the legal concentration authorized for marketing by the Food and Drug Administration (FDA) and the Pharmaceutical Administration of the Ministry of Health and Welfare of Japan. Thus, the purpose of this systematic review and meta-analysis is to get additional insight into the safety and effectiveness of topical 0.05% clobetasol cream in the management of CHE.

❖ Efficacy of Clobetasol Propionate in CorticosteroidResponsive Dermatoses

1.Atopic dermatitis

Common in nonage, atopic dermatitis(announcement) is characterized by itching and xerosis with intermittent occurrences of relapse and retrogression. The maturity of announcement is moderate and treatable with emollients; new topical calcineurin impediments or topical corticosteroids are the primary treatments. numerous exploration have assessed the effectiveness of CP in treating announcement. When children get one diurnal operation of CP0.05 without occlusion, their tube cortisol situations drop, analogous to what happens with other strong topical steroids.69. Healing was reported in a lesser chance of cases treated with halobetasol propionate ointment than in the clobetasol propionate treatment group(65.1 versus54.7) in a double-eyeless, resemblant- group, multicenter relative trial involving 127 evaluable cases with habitual, localized atopic dermatitis or lichen simplex chronicus. Despite this, the two remedy groups' overall success rates(93.7 versus92.2) and early remedial benefit inception(within 3 days of treatment inauguration) and side goods were nearly equal.[35]. Seventy When CP emollient cream is used in confluence with the vehicle, two studies show that it's largely effective in treating moderate- to-severe atopic dermatitis.[36, 37]In order to treat moderate to severe announcement, a comparison exploration was conducted on 229 cases using the CP emollient cream expression and a embrocation vehicle administered doubly daily for two weeks. In comparison to clobetasol propionate emollient cream, embrocation was shown to be more efficient, safe, well-permitted, and to have a better absolution profile in thismulti-center, randomized, active- and vehicle- controlled, investigator- dazed exploration.[38]. The safety and effectiveness of CP conflation froth0.05 in treating steroid-responsive dermatoses across a range of age groups were assessed by Kimball and coll. 52 individualities with mild-to-severe atopic dermatitis(announcement) who were 6 times of age or aged shared in a phase II open- marker trial to assess the effect. 32 individualities with mild- to-moderate shrine- type psoriasis who were 12 times of age or aged shared in another phase II open- marker pharmacokinetic safety exploration. Actors with mild- to-moderate shrine-type psoriasis(N = 497) or moderate- to-severe announcement(N = 377) who were 12 times of age or aged were estimated for treatment efficacity in two phase III, randomized controlled trials. Actors entered the study drug for two weeks in eachstudy.Treatment effectiveness was assessed using similar measures in the announcement and psoriasis studies, and a change of at least two grades from the birth was supposed noteworthy. When using clobetasol froth rather of vehicle froth, a significantly advanced chance of actors completed their treatment, and reversible HPA repression was seen in 27 of actors who were 18 times of age or aged, 47 of actors who were between the periods of 6 and 12 times, and 0 of actors who were between the periods of 12 and 15 times. The results supported the earlier conclusions that children youngish than two times old shouldn't admit CP or other class I topical corticosteroids.[39]

2.Lichen sclerosus genitalis

Prepubertal girls, adult and postmenopausal females, and elderly males can all develop lichen sclerosus (LS), an inflammatory skin condition with an unclear cause that affects the anogenital area. It may be linked to the emergence of squamous cell carcinoma in people who are adults.

Although many individuals with lichen sclerosus respond well to extremely strong topical steroids, questions remain over their long-term safety. Two small-scale studies examined the effectiveness of a regimen based on CP ointment 0.05% in girls, showing excellent results with 4-week and 8-week treatment periods. However, frequent recurrences and the risk of atrophy required the doctor to perform ongoing observation every 6 to 12 months in order to monitor recurrences and complications that could leave scars.[40, 41]Since 1990, reports on the management of vulval LS in adult females with CP have been made.[42,43]The effectiveness of CP in relation to tes-tosterone proprionate 2% was

examined in further research. Although no discernible improvement was seen in terms of clinical features and histological abnormalities, as was the case with CP without any notable side effects, testosterone was found to have a good efficacy in respect to symptoms.[44] in Another study found that in both remission induction and maintenance therapy, clobetasol 17-propionate 0.05% was superior to testosterone.[46] Four topical medications were used for three months: clobetasol propionate (0.05%), progesterone (2%), testosterone (2%), and cream-based preparation. The trial involved 79 patients with vulval LS who were treated randomly.

Comparing clobetasol-treated patients to other treatment groups, the former showed superior response. 25% of CP patients receiving testosterone treatment, 10% receiving progesterone treatment, and 10% receiving a cream-based preparation experienced symptom remission. In contrast, 75% of CP patients receiving treatment experienced this outcome.[45]Treatment for vulvar lipomatosis (LS) for both short and long periods was assessed in two groups of 20 patients, using topical testosterone propionate 2% in petrolatum against CP 0.05%. The 3-month follow-up revealed a similar level of efficacy, but the 1-year follow-up revealed a greater level of CP efficacy. The 87 According to Cattaneo and Coll, using testosterone for an extended period of time seemed to have a negative impact following the positive effects of CP cream use for 24 weeks.No.[46]

In 81 consecutive individuals with biopsy-proven vulvar LS, a retrospective chart review research revealed a 77% chance of full symptom resolution and a 47% chance of improvement in the vulva's clinical appearance when using clobetasol.89 CP treatments lasting longer than 12 weeks were examined in 137 women with severe vulvar LS who were either treated "as required" or on a regular basis for a period of six months. At two, three, six, and twelve months after starting treatment, every patient was evaluated. When it came to their symptoms, 59% of the first group and 85% of the second had a complete response in the 6-month follow-up, while the corresponding numbers on the 12-month follow-up were 48% and 74%.

After using CP 0.05% for an extended period of time, no negative effects were noted.Nineteen In a prospective study that took place between 1981 and 2001, 83 women with vulvar LS were treated until they achieved complete clinical and histologic remission. The women were then monitored for signs of clinical and histologic recurrence (with a median follow-up of 4.7 years) to determine the likelihood that they would develop squamous cell carcinoma. For 45 patients, or 54%, complete remission was achieved. Age had a strong correlation (P = 0.001) with the likelihood of remission. At three years, the estimated incidence of remission was 0% in women over seventy years old, 23% in those between fifty and seventy years old, and 72% in those younger than fifty.

Relapse rates were calculated to be 50% at 16 months and 84% at 4 years. Age did not influence the occurrence of relapses. Due to the disease's protracted progression, treatment with a strong steroid cream appeared to help but not cure VLS in women older than 70. Although the authors suggested that there may be a protective effect from malignant evolution, the number of patients who appeared to be protected from malignant evolution was too small to be statistically significant, and 8 vulvar squamous cell carcinomas (9.6%) were found in lesions that had either never been treated before or had been treated irregularly.Nineteen 292 patients receiving CP treatment for clinically typical or biopsy-confirmed vulvar LS were included in a large population study. Of these patients, 75% had consultations or had their charts examined retrospectively.

Though 85% of patients needed long-term, intermittent treatment, topical CP was demonstrated to be quite helpful in this regard. Twenty-two (12%) of the 185 patients who were followed up still had moderate-to-severe symptoms, while 101 (56%) of the patients showed no symptoms at all.[47].On 83 women with vulvar LS who had varying degrees of squamous cell hyperplasia (mixed disease), a retrospective research was carried out. Sporadic fluorinated corticosteroids were administered to all patients initially, followed by either 0.05% clobetasol 17-propionate or 2% testosterone propionate in petrolatum (44 (53%) versus 39 (47%)). After six months (p = 0.112), the remission rates for the testosterone and clobetasol subgroups were 82 and 93%, respectively. Even while statistically significant differences were not found, 8% of the patients experienced a recurrence of the disease, with greater rates in the testosterone arms.903 With no risk of epidermal atrophy and a slight chance of causing latent infections, including

human papillomavirus, topical clobetasol propionate treatment offered a safe and effective therapy for penile LSA as well.[48]

3.Boullous autoimmune skin dermatoses

Bullous skin conditions can have an autoimmune base, be acquired or caused, or both. Autoantibodies that target specific adhesion motes of the dermoepidermal basement membrane zone and epidermis are present in all autoimmune bullous skin conditions. These antibodies beget the targeted protein's tenacious rates to be lost, which ultimately causes pocks and attritions to show up. Autoimmune bullous or vesiculo- bullous skin diseases are more common in women, just as utmost other autoimmune conditions. Westerhof published the first study on the effectiveness of CP in treating autoimmune bullous illness in1989.[49] In a posterior study, JolyP. And coll aimlessly assigned 341 cases to admit oral prednisone(0.5 mg per kilogram of body weight per day for cases with moderate complaint and 1 mg per kilogram per day for cases with expansive complaint) or topical clobetasol propionate cream(40 g per day). Topical corticosteroids were superior to oral prednisone(P = 0.02) in the 188 cases with expansive bullous pemphigoid. The oral prednisone group had a one- time survival rate of 58, while the topical corticosteroid group had a rate of 76. The study's conclusions supported the effectiveness of CP for both moderate and severe cases of bullous pemphigoid, and they showed superiority over oral corticosteroid remedy for cases with expansive illness with quicker complaint control and less serious sideeffects.In a multicenter randomized controlled trial, it was also shown that 106 superpotent topical corticosteroids bettered the survival of cases with bullous pemphigoid complaint(BP), with 312 individualities being stratified grounded on the inflexibility of their BP. A normal authority(40 g of clobetasol propionate cream per day originally, with CS tapering over 12 months) and a light authority(10 – 30 g per day, with CS tapering over 4 months) were compared. Using the light authority of156/159(98) vs the usual authority of150/150(100; P = 0.005), a noninferior rate of blood pressure control was achieved. The combined outgrowth of deaths and life- hanging adverse events didn't differ between the two treatment groups in terms of event-free survival(P = 0.77). But when age and Karnofsky score were taken into account using the Cox model, cases showed a significant benefit from the light authority. Compared to the usual authority, there's nearly a twofold reduction in the threat of death or life- hanging adverse events with moderate blood pressure.[50,51] In confluence with antibiotics and/ or antimycotic ointments for Hailey- Hailey Pemphigus, as well as effective when used alone for moderate Pemphigus vulgaris with prolonged absolution in a specific case group, the use of CP appears to ameliorate the clinical efficacity of systemically administered dapsone inBP.[52, 53]

❖ ADR Reports on Clobetasol propionate[54]

- Blood and lymphatic system disorder (0%,58 ADRs)
- Cardiac disorders (0%,58 ADRs)
- Congenital,familial and genetic disorders (0%,22 ADRs)
- Ear and labyrinth disorders (0%,32 ADRs)
- Endocrine disorders (2%,275 ADRs)
- Eye disorders (2%,286 ADRs)
- Gastrointestinal disorders (2%,363 ADRs)
- General disorders and administration site conditions (31%,4890 ADRs)
- Hepatobiliary disorders (0%,16 ADRs)
- Immune system disorders (1%,185 ADRs)
- Infections and infestations (4%,597 ADRs)
- Injury, poisoning and procedural complications (11%,1811 ADRs)
- Investigations (2%,385 ADRs)
- Metabolism and nutritional disorders (1%,171 ADRs)
- Musculoskeletal and connective tissue disorders (4%,661 ADRs)
- Neoplasms benign, malignant and unspecified (incl cysts and polyps) (1%,228 ADRs)
- Nervous system disorders (4%,696 ADRs)

- Pregnancy, puperium and perinatal conditions (0%,28 ADRs)
- Product issues (2%,363 ADRs)
- Psychiatric disorders (2%,367 ADRs)
- Renal and urinary disorders (1%,83 ADRs)
- Reproductive system and breast disorders (1%,116 ADRs)
- Respiratory, thoracic and mediastinal disorders (1%,162 ADRs)
- Skin and subcutaneous tissue disorders (23%,3674 ADRs)
- Social circumstances (0%,63 ADRs)
- Surgical and medical procedures (0%,40 ADRs)
- Vascular disorders (1%,167 ADRs)

❖ Geographical distribution

Continent	Count	Percentage
Africa	32	0
Americas	5538	65
Asia	1704	20
Europe	1284	15
Oceania	27	0

❖ Patient sex distribution

Sex	Count	Percentage
Female	4661	54
Male	3109	36
Unknown	815	9

❖ Age group distribution

Age group	Count	Percentage
0-27 days	9	0
28 days to 23 months	34	0
2-11 years	89	1
12-17 years	157	2
18-44 years	1618	19
45-64 years	1248	15
65-74 years	572	7
≥75 years	490	6
Unknown	4368	51

❖ ADR Reports as per year

Year	Count	Percentage
2024	391	5
2023	3179	37
2022	576	7
2021	513	6
2020	428	5
2019	630	7
2018	511	6
2017	412	5
2016	293	3
2015	328	4
2014	312	4
2013	126	1
2012	252	3
2011	151	2
2010	87	1

2009	24	0
2008	56	1
2007	2	0
2006	17	0
2005	32	0
2004	18	0
2003	7	0
2002	9	0
2001	14	0
2000	18	0
1999	9	0
1998	6	0
1997	14	0
1996	12	0
1995	20	0
1994	18	0
1993	10	0
1992	22	0
1991	8	0
1990	10	0
1989	16	0
1988	15	0
1987	4	0
1986	5	0
1985	4	0
1984	3	0
1983	1	0
1982	2	0
1981	2	0
1980	1	0
1979	4	0
1978	3	0
1977	5	0
1976	4	0
1975	1	0

Current data set date is 01/04/2024. The dataset is normally updated on Sundays at CET (± 1 hour)

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