Comparative effectiveness of Topical Calcipotriol and Topical Betamethasone Valerate in Mild and Moderate Plaque Type Psoriasis. An Open-Labelled Comparative Study

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ABSTRACT:

Background: Plaque-type psoriasis is a chronic inflammatory dermatosis type condition.

Aim/ Purpose: To assess the beneficial effects of topical Calcipotriol (0.005%) ointment when applied to mild and moderate plaque-type psoriasis.

Material and Methods: 80 patients with plaque-type psoriasis were included in an open-label, comparative 90-day case study at Dermatology Department at Jinnah Postgraduate Medical Centre (JPMC), Karachi, These patients have divided into two groups: group A received topical Betamethasone valerate (0.1 percent) ointment and group B received topical Calcipotriol (0.005 percent) ointment, with 20 patients in each mild and moderate plaque-type psoriasis. The PASI score, adverse effects, and serum calcium level were used to measure improvement in plaque-type psoriasis patients.

Results: This open-label comparative study on plaque-type psoriasis was evaluated using the Psoriasis Area and Severity Index (PASI) scores. PASI scores improved in patients with mild and moderate plaque-type psoriasis who received topical Calcipotriol ointment and topical Betamethasone valerate ointment. Skin irritation was more common in group-B patients with mild to moderate plaque-type psoriasis who received topical Calcipotriol ointment, but burning sensations, rashes, and telangiectasia were more common in group-A patients with mild to moderate plaque-type psoriasis who received topical Betamethasone valerate ointment. There was no significant difference in serum calcium levels in both the groups that received topical Betamethasone valerate and topical Calcipotriol ointments at day 30, 60 and 90.

Conclusion: Calcipotriol had better results in mild and moderate plaque-type psoriasis than Betamethasone valerate when given topically, with lower PASI scores and fewer side effects.

Keywords: Plaque type psoriasis, Betamethasone valerate ointment, Calcipotriol ointment, Psoriasis Area Severity Index (PASI) score, serum calcium level.

INTRODUCTION:

Psoriasis is a chronic inflammatory skin condition that affects 2–3% of the world's population. The prevalence in the tropical region is low while Scandinavian regions have a high prevalence of up to 11% [1, 2].

Both genders are equally affected at any age, demonstrating that the onset of Psoriasis is not affected by age or gender [3]. The pathophysiology of psoriasis has been linked to both genetic and environmental factors. About 45% of Psoriatic patients have a family history of the condition [4]. Psoriatic patients under the age of 20 show a high level of genetic involvement [5]

Psoriasis vulgaris, often known as Plaque Psoriasis, appears to be the most common kind of Psoriasis, accounting for 80 to 90% of all cases [6].

Psoriasis is a widespread, chronic inflammatory skin condition marked by circular, confined, erythematous, dry, scaling plaques of varied diameters coated in greyish white or silvery white scales [7].This inflammatory auto-immune disease affects significant areas of the skin and is most typically seen on the scalp, trunk, and extensor sides of the upper and lower limbs [8].

There is currently no cure for Psoriasis, thus treatment focuses on reducing Psoriatic lesions and alleviating accompanying symptoms [9]. Topical drugs, such as corticosteroids, vitamin D analogues, vitamin A analogues, and coal tar preparations, are commonly used to treat mild-to-moderate Psoriasis vulgaris, which accounts for the majority of cases of the disease. Topical therapies for psoriasis are usually effective and safe when used correctly [10]. In a comprehensive review, de Jager et al. concluded that topical treatment with Calcipotriol, if necessary, along with topical corticosteroids should be the treatment of choice in mild or moderate Psoriasis [11]. In most cases, topically applied drugs effectively treat mild and severe Plaque Psoriasis [12, 13].

Betamethasone valerate, a synthetic medium-potent glucocorticoid, is an anti-psoriatic medication that works by slowing the growth of dead skin cells and lowering inflammation in Psoriatic lesions [14]. Calcipotriol, a synthetic Vitamin D analogue, works as an anti-psoriatic medication by inhibiting psoriatic keratinocyte growth and aberrant differentiation [15].

The adverse effects of topical Betamethasone valerate ointment include burning sensations, rashes, and telangiectasia, whereas topical Calcipotriol ointment is usually associated with skin irritation [16].

Calcipotriol is a new and effective topical therapy for psoriasis vulgaris with persistent plaques. Because it's an analogue of calcitriol (1,25 dihydroxyvitamin D, the active metabolite of vitamin D), it can alter systemic calcium metabolism even when applied topically. Serum calcium levels were unfavourably influenced in patients with mild and moderate plaque type psoriasis who used topical Calcipotriol ointment [17].

There is some evidence that Calcipotriol is harmful even when administered at prescribed levels. It may cause a rise in urine calcium, which, if used long-term, can lead to renal calculi [18, 19].

The focus of this research was to determine the safety profile of Calcipotriol and its effect on systemic calcium homeostasis in patients with mild to moderate plaque psoriasis.

The efficiency and safety characteristics of topical Betamethasone valerate ointment and topical Calcipotriol ointment are associated when used alone. As a result, the objective of this study was

to see how beneficial topical Calcipotriol (0.005%) ointment was in treating mild and moderate Plaque type Psoriasis.

MATERIAL AND METHODS:

The comparative, open labelled case study was conducted in Jinnah Postgraduate Medical Centre, in the Pharmacology and Therapeutics department of Basic Medical Science Institute (BMSI) in Karachi for 90 days. After selection and randomization by lottery method, 80 plaque type psoriasis patients were divided into two groups: Group A: received topical Betamethasone valerate (0.1%) ointment, 20 patients in each mild and moderate Plaque type Psoriasis, and Group B received topical Calcipotriol (0.005%) ointment, 20 patients in each mild and moderate Plaque type Psoriasis.

The participants in this case study ranged in age from 20 to 60 years old and had mild to moderate Plaque type Psoriasis. Patients with scalp plaque type psoriasis, severe plaque type psoriasis, liver/ renal disease, multiple skin disorders, hypersensitivity to given case study drugs, expecting/breast-feeding mothers, and those who had taken given case study drugs within a month prior to this case study were excluded.

The PASI score, adverse effects, and serum calcium level were used to measure improvement in Plaque type Psoriasis patients.

The Psoriasis Area and Severity Index (PASI) is the most commonly suggested technique for evaluating Psoriatic lesions. The severity of Psoriatic lesions is determined by the three clinical indicators of redness (erythema), thickness (induration), and scaling (desquamation). The PASI score ranges from 0 (no disease) to 72 (maximal disease), showing the extent to which psoriasis has affected the body [20]

The sample size of psoriatic patients was calculated using Open Epi version 16, and all study values were evaluated as mean and SEM using SPSS 20. Under the null hypothesis, the p-value < 0.05 was considered significant. Eighty patients were divided into two groups: Group A received topical Betamethasone valerate ointment and Group B received topical Calcipotriol ointment, with forty patients in each group. Each group was separated into sub-groups of mild and moderate plaque type psoriasis, with twenty patients in each sub-group as shown in **Table 1**, based on the severity of the skin disease.

Table 1: GROUPING OF PATIENTS

Drugs	Groups	Grading of plaque type psoriasis	Number of patients (n)
Topical Betamethasone valerate ointment	A	Mild	20
		Moderate	20
Topical Calcipotriol ointment	B	Mild	20
		Moderate	20

RESULTS:

For a 90-day case study, eighty patients with mild and moderate plaque type psoriasis were treated topically with Betamethasone valerate and Calcipotriol ointments.

Table 2: Comparison in mean PASI score from day-0 to day-90 between Group-A and Group-B patients of mild and moderate plaque type psoriasis

Group	Mean PASI Score (day- 0)	Mean PASI Score (day-90)	p-value
Mild Psoriasis			
Group–A Betamethasone valerate	8.45±0.17	3.11 ±0.26	0.37
Group–B Calcipotriol	8.70 ±0.11	2.47±0.12	
Moderate Psoriasis			
Group–A Betamethasone valerate	15.80 ±0.54	6.25±0.40	0.46
Group–B Calcipotriol	16.40 ±0.45	5.05 ±0.14	

Values are expressed in mean ± SEM
SEM = Standard Error of Mean, p-value - <0.05

When comparing group-A patients with mild plaque type psoriasis who received topical Betamethasone valerate ointment to group-B patients with mild plaque type psoriasis who received topical Calcipotriol ointment, it was clear that those who received topical Calcipotriol ointment change in PASI score with a reduction in mean PASI score level from 8.70 ±0.11 at day 0 to 2.47±0.12 at day 90 than those patients who took topical Betamethasone valerate ointment and revealed change in PASI score with a decline in mean PASI score level from 8.45±0.17 at day 0 to 3.11±0.26 at day 90.

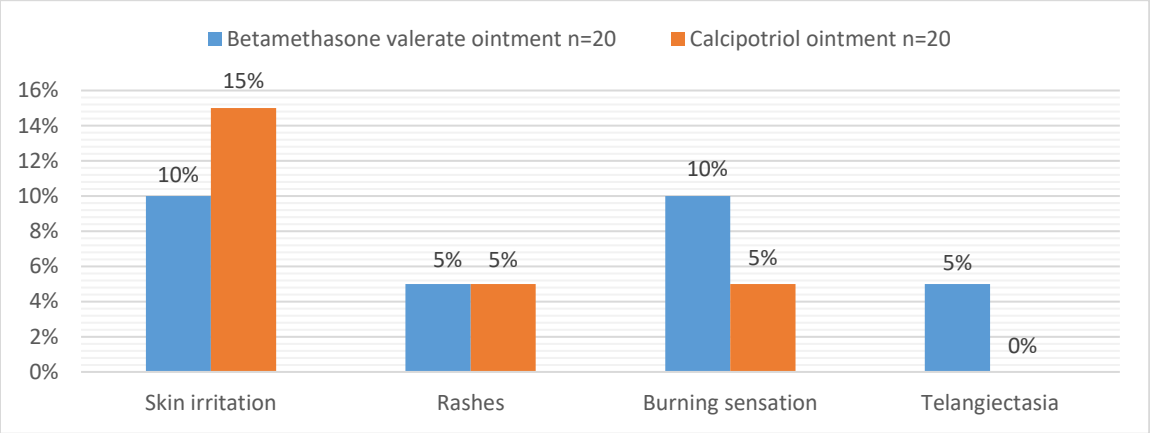
Then, when group-A patients with moderate plaque type psoriasis who received topical Betamethasone valerate ointment were compared to group-B patients with moderate plaque type psoriasis who received topical Calcipotriol ointment, those who took topical Calcipotriol ointment showed a decrease in mean PASI score level from 16.40 ±0.45 at day 0 to 5.05 ±0.14 at day 90 than those patients who received topical Betamethasone valerate ointment showed a decline in PASI score with a drop in mean PASI score level from 15.80±0.54 at day 0 to 6.25±0.40 at day 90.

On day 90, there were no significant changes in p-values between patients with mild and moderate plaque type psoriasis between groups A and B, as indicated in **Table 2.**

Adverse effects such as skin irritation and burning sensation were discovered in 2 (10%) of the 20 patients in Group A, who had mild plaque type psoriasis and were treated with topical Betamethasone valerate ointment, while rashes and telangiectasia were found in 1 (5%) of the

patients. Skin irritation was discovered in three (15%) of the 20 patients in Group-B who had mild plaque type psoriasis and were treated with topical Calcipotriol ointment, while rashes and burning sensation were seen in one (5%) patient each, but no patient had telangiectasia, as shown in **Figure 1.**

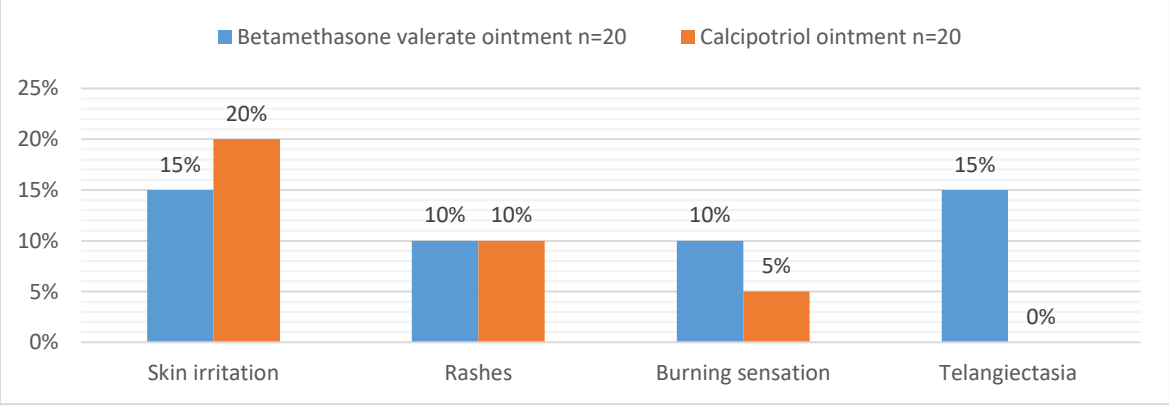
Figure-1: Comparison of Adverse effects between Group-A and Group-B patients with mild Plaque type Psoriasis



Legend: Skin irritation was the most common adverse effect in both the Groups. Also burning sensation was also observed in Group A patients**.**

Skin irritation was detected in 3 (15%) of the 20 patients in group A who were treated with topical Betamethasone valerate ointment for moderate plaque type psoriasis. Rashes and burning sensation were observed in 2 (10%) of the patients. Telangiectasia was present in 3 (15%) of the individuals. Skin irritation was seen in 4 (20%) of the 20 patients in group B who had moderate plaque type psoriasis and were treated with topical Calcipotriol ointment. Rashes were seen in two (10%) of the patients. As seen in **Figure-2**, one patient (5%) experienced a burning sensation, whereas none of the others were impacted by telangiectasia.

Figure-2: Comparison in Adverse effects between Group-A and Group-B patients of Moderate Plaque type Psoriasis



Legend: Skin irritation was the most common adverse effect in both the Groups. Telangiectasia was another adverse observed in Group A patients.

In mild plaque type psoriasis, the mean serum Calcium level at day 0 in group-B patients (n=20) treated with topical Calcipotriol ointment was 8.36 ± 0.05 mg/dl, increased to 8.40±0.05 mg/dl at day 30, improved to 8.50 ± 0.05 mg/dl at day 60, and declined to 8.40 ± 0.49 mg/dl at day 90. The percentage change and mean serum Calcium level were statistically non-significant when compared from day 0 to day 90, as shown in the Table 3.

In moderate Plaque type Psoriasis patients, the mean serum Calcium level at day 0 was 8.67±0.10 mg/dl in 20 patients of group-B who were treated with topical Calcipotriol ointment, increased slightly to 8.70±0.10 mg/dl at day 30, reduced to 8.66±0.10 mg/dl at day 60, and decreased to 8.64±0.10 mg/dl at day 90. The percentage change and mean serum Calcium level were statistically non-significant when compared from day 0 to day 90, as shown in **Table 3**.

Table 3: Changes in mean serum calcium level (mg/dl) in group-B patients of mild and moderate plaque type psoriasis taking topical Calcipotriol ointment

Days	Mean Serum Calcium Level (mg/dl)	Percentage Change	p-value
Mild Psoriasis			
Day 0	8.36 ±0.05	-0.42%	0.089
Day 30	8.40 ±0.05		
Day 30	8.40 ±0.05	-0.19%	0.065
Day 60	8.50 ±0.05		
Day 60	8.50 ±0.05	0.08	0.287
Day 90	8.40 ±0.49		
Day 0	8.36 ±0.05	-0.48%	0.072
Day 90	8.40 ±0.49		
Moderate Psoriasis			
Day 0	8.67±0.10	-0.35%	0.186
Day 30	8.70±0.10		
Day 30	8.70±0.10	0.09%	0.176
Day 60	8.66±0.10		
Day 60	8.66±0.10	0.02%	0.267
Day 90	8.64±0.10		
Day 0	8.67±0.10	0.33%	0.309
Day 90	8.64±0.10		

Values are expressed in mean ± SEM
SEM = Standard Error of Mean, p-value - <0.05

DISCUSSION:

Between Day 0 (baseline) and Day 90 (end of therapy), a decrease in the mean PASI score was observed in a three - month case study on topical Betamethasone valerate ointment (group-A) and topical Calcipotriol ointment (group-B).

Fujiyama T. et al. (2016) reported comparable findings, stating that topical Calcipotriol and topical Betamethasone ointment, when given for two weeks with equivalent severity, normalize psoriatic changes in different ways [21].

In another study, the comparison was conducted over the course of four weeks. The percentage reduction in the PASI score at week 1 and week 4 was measured. At any time point, no statistically significant changes in the outcome was found between the two topical therapeutic approaches (P = 0.3 and P = 0.052)[9].

Dahri et al. found that the PASI parameter in Calcipotriol improved, with a significant mean change from14.08±0.33 to 4.52±0.22 [22]

In the current trial, Perilesional skin irritation was the most common adverse effect of Calcipotriol, but it was rarely severe enough to need treatment discontinuation.

According to J Coo et al., Arijit Coondoo et al. and Papp KA et al., skin irritation was slightly more common in patients treated with topical Calcipotriol ointment, while other possible adverse effects such as rashes, burning sensation, and telangiectasia were more common in patients treated with topical Betamethasone valerate ointment in mild and moderate plaque type psoriasis [23-25].

In a single-center, randomized study of 26 individuals with scalp psoriasis, the most common adverse drug events associated to topical steroid treatment were erythema, telangiectasia, skin rash, and skin atrophy [26].

In this investigation, telangiectasia was identified in betamethasone-treated participants. According to a study, it was elaborated that telangiectsia is frequent with steroid than Vitamin D analogues and Steroid-induced telangiectasia occurs when the release of nitric oxide from cutaneous artery endothelial cells is triggered, causing abnormal capillary dilation [27].

The present study shows that in mild to moderate psoriasis, there was no significant change in serum calcium levels after 30 days, 60 days, or 90 days. When the prescribed dosage (100 grams/week) of topical Calcipotriol ointment was applied, Shepard et al. (2007) found no significant change in serum Calcium levels, supporting safety in hypercalcemic patients with mild and moderate plaque type psoriasis.

A study mentioned that for mild to moderate chronic plaque psoriasis, topical calcipotriol is a safe and efficient treatment. Serum total adjusted calcium should be evaluated on a regular basis in individuals with more severe psoriasis who take dosages approaching the maximum advised dose of calcipotriol. If serum ionized calcium is available, it can potentially be utilized to detect toxicity early[28].

CONCLUSION:

It was concluded that Calcipotriol (0.005%) has a better safety profile than betamethasone (0.1%) in the treatment of mild and moderate plaque type psoriasis. Both groups experienced adverse effects, especially in the early stages of treatment. However, these were minimal side effects, and no patients had to stop therapy because of them, and all the adverse effects remitted spontaneously without treatment during the study period.

STATEMENTS AND DECLARATIONS:

Conflicts of Interest: None

We now confirm that all of the manuscript's Figures and Tables are our own.

Ethical Clearance: The project was approved by the University local ethical council.

AUTHORS CONTRIBUTION STATEMENT:

SI designed and managed the research and UN performed the experiments. LF and UZ examined the data and analyzed the results; MS and ML established the theoretical framework and wrote the article. The results were evaluated by all authors, and the final version of the manuscript was approved.

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