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A comparative study of efficacy and safety of topical calcipotriol and topical dithranol in chronic plaque psoriasis

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Abstract

Background: Psoriasis is chronic inflammatory dermatosis with genetic background. Topical therapy alone is effective in localized psoriasis
Objective: Study was conducted to compare the efficacy and safety of topical calcipotriol and dithranol in mild chronic plaque psoriasis with less than 10% BSA involvement
Methods: Study duration was 6 weeks. Thirty patients each were included in two groups. In calcipotriol group, patients applied calcipotriol ointment (0.005%) twice daily. In dithranol group patients applied 1% ointment in 1st week, 2% ointment during 2nd week, 3% ointment from 3rd weeks onwards. Duration of application was 60 minutes, once daily.
Results: Patients responded to both the treatments satisfactorily. However, calcipotriol was superior in efficacy. Patients in both the groups tolerated the treatment.
Conclusion: Both calcipotriol and dithranol (short contact therapy) were effective in the treatment of mild chronic plaque psoriasis. Even though, dithranol is less potent, it is cost effective.

Keywords: Plaque psoriasis, calcipotriol, dithranol

Introduction

Psoriasis is a common genetically mediated chronic inflammatory dermatosis. Psoriasis with limited body surface involvement can be managed by application of topical agents. Apart from topical steroids, coal tar, dithranol, vitamin D3 analogues, topical calcineurin inhibitors are prescribed with good efficacy. Dithranol is applied as short contact therapy (SCAT) which entails application of anthralin for 20 to 60 minutes [1]. Satisfactory results are seen after 4-6 weeks of application. However, anthralin appears to have lower efficacy than calcipotriol [2].
Vitamin D analogues are very useful topical agents in the treatment of chronic plaque psoriasis. It can be combined with dithranol, narrow band NBUVB for better efficacy [3].

Objectives

To evaluate and compare the efficacy and safety of topical calcipotriol and topical dithranol in patients suffering from chronic plaque psoriasis.

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Methods

The study was conducted on sixty patients of chronic plaque psoriasis attending dermatology OPD of teaching hospital located in Bengaluru between September 2017 and September 2019.

Inclusion criteria

Both male and female patients of all age groups.
Patients having psoriasis which was confirmed by lesional skin biopsy.
Body surface area involvement less than 10%.

Exclusion criteria

1. Patients of psoriasis other than plaque type of psoriasis.
2. Patient with renal dysfunction, renal calculi, underlying condition that required use of calcium and vitamin D supplements.
3. Patients who had used topical anti psoriatic medication within past 2 weeks or had used systemic anti psoriatic medication within past 4 weeks.
4. Pregnant women.

Method

A total of sixty patients of chronic plaque psoriasis were selected based on inclusion and exclusion criteria and were recruited for the study. These 60 patients were divided into two groups, calcipotriol group and dithranol group with 30 patients in each group and were assigned alternatively.

Calcipotriol group: Patients in this group were treated with topical calcipotriol 0.005% or 50 μg/gram ointment applied twice daily for 6 weeks, or until lesions were resolved, whichever was earlier.

Dithranol group: Patients in this group with topical dithranol ointment with increasing strengths from 1% ointment for first week, 2% ointment for 2nd week, 3% ointment from 3rd week onwards, applied once daily for 60 minutes for a total period of 6 weeks or till lesions resolved, whichever is earlier. The skin around the lesions were smeared with Vaseline to prevent possible irritation.
Patients underwent efficacy and safety evaluation every week from baseline (week 0) until week 6 or until lesions resolved which ever was earlier

Assessment of efficacy: It was done by:

1. Global assessment of improvement
2. Dermatological sum score (DSS)
3. Psoriasis area severity index score (PASI).

1. Global assessment of improvement included objective and subjective score. Maximum efficacy score was 3 (Clear or almost clear) (Scale of 0-3).
2. A scale of 5 was employed to assess erythema, plaque elevation and scale to determine dermatological sum score.
3. Four sites were selected (Head, trunk, upper limb, lower limb) to assess PASI score.
4. All the assessments were carried at baseline and every week for 6 weeks.

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Assessment of safety: It included:

1. Clinical assessment of cutaneous safety
2. Assessment of cutaneous discomfort

Cutaneous assessment on the scale of 5 (0-4) was employed to study local irritation.
Same scale of 0-4 (No discomfort to very severe discomfort) was used in the study to assess cutaneous discomfort.
All the assessments were carried at baseline and every week for 6 weeks.
Institution ethical committee approval was taken (MVJMC&RH/Adm /ECM/2017-18) dated 12-10-2017
Informed consent was obtained from patients recruited in the study.
Unpaired t-test was employed to compare the findings.

Results

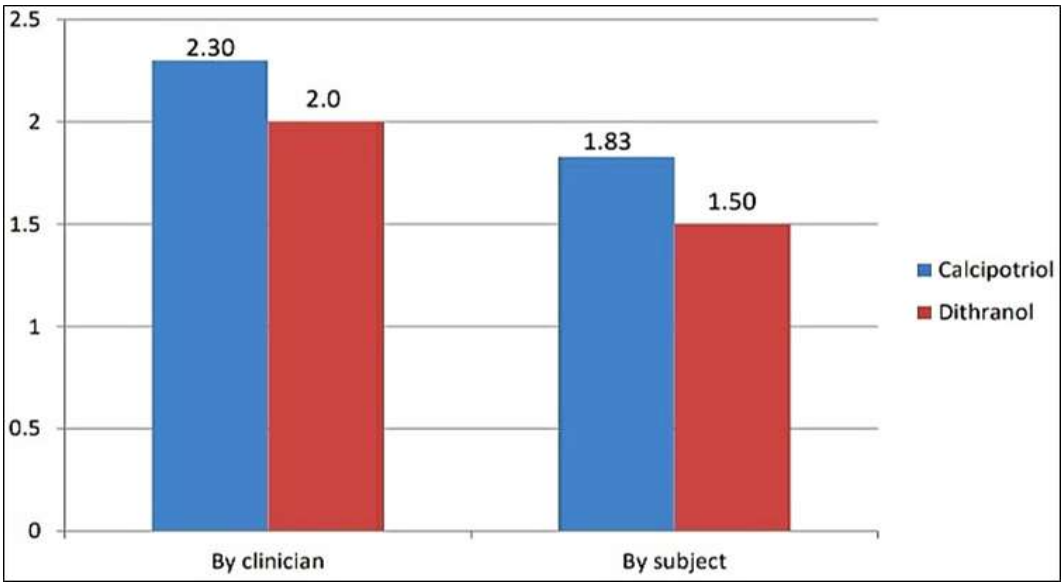
In this study, majority of patients belonged to age group of 31-40 years (calcipotriol group), 41-50 years (dithranol group) which was statistically not significant.
Both calcipotriol group (66.7%), dithranol group (56.7%) demonstrated male predominance.
The majority of cases in calcipotriol group (43.33%) had a BSA involvement of 1-3% and that in dithranol group (43.33%) had a BSA involvement of 4-7%. Which was comparable in both the groups.
The duration of psoriasis was 1-6 months in 53.3 (calcipotriol), 46.7% (dithranol group) which was statistically not significant.
Both physician and patient global assessment were similar Calcipotriol showed superior efficacy 40% v/s 26.6% (clinician assessment, as well as patient assessment (16.7%v/s 13.4%).
The baseline DSS did not show statistically significant difference ($p>0.05$) between the two groups and hence both the groups were comparable. The reduction of DSS in calcipotriol group at week 6 compared to baseline was found to be statistically significant ($p<0.05$).
The reduction of DSS in dithranol group at week 6 compared to baseline was found to be statistically significant ($p<0.05$).
On comparing DSS of both groups, there was statistically significant difference between calcipotriol group and dithranol group in the reduction of DSS favouring calcipotriol at week 4, week 5 and at week 6 of treatment.
The baseline PASI score did not show statistically significant difference between the two groups ($p>0.05$).
The reduction of PASI score in calcipotriol group at week 6 compared to baseline was found to be statistically significant.
The reduction of PASI score in dithranol group at week 6 compared to baseline was found to be statistically significant.
On comparing PASI scores of both groups, there was statistically significant difference between calcipotriol group and dithranol group in the reduction of PASI scores favouring calcipotriol at week 4, week 5 and at week 6 of treatment. [Table 1]
Overall, the global improvement was seen in both calcipotriol group and dithranol group [Graph 1, Figures 1, 2, 3, 4].

Table 1: PASI score comparison between calcipotriol group and dithranol group

	Calcipotriol Group Mean PASI score ± SD	Dithranol Group Mean PASI score ± SD	p value
Week 1	2.12 ± 1.02	2.11 ± 0.90 (1% Dithranol)	0.94
Week 2	1.62 ± 0.88	1.77 ± 0.83 (2% Dithranol)	0.48

Week 3	1.18 ± 0.72	1.41 ± 0.71(3% Dithranol)	0.22
Week 4	0.73 ± 0.49	1.12 ± 0.61(3% Dithranol)	0.009
Week 5	0.34 ± 0.29	0.80 ± 0.53(3% Dithranol)	<0.0001
Week 6	0.09 ± 0.14	0.35 ± 0.30(3% Dithranol)	<0.0001

Unpaired t-test; p<0.05-significant, p 0.05-Non-significant.



Graph 1: Global assessment of improvement compared between calcipotriol group and dithranol group

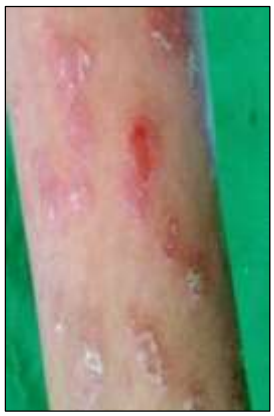


Fig 1: Baseline photo of the patient treated with calcipotriol

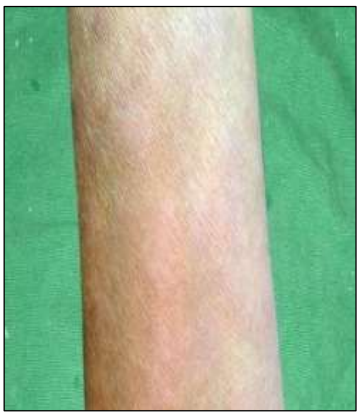


Fig 2: Clinical photo after 6 weeks of treatment with topical calcipotriol

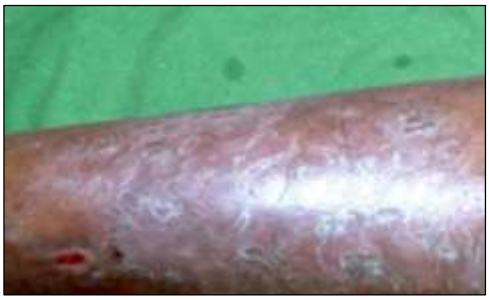


Fig 3: Baseline photo of the patient treated with dithranol

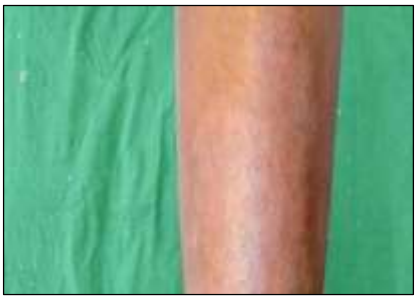
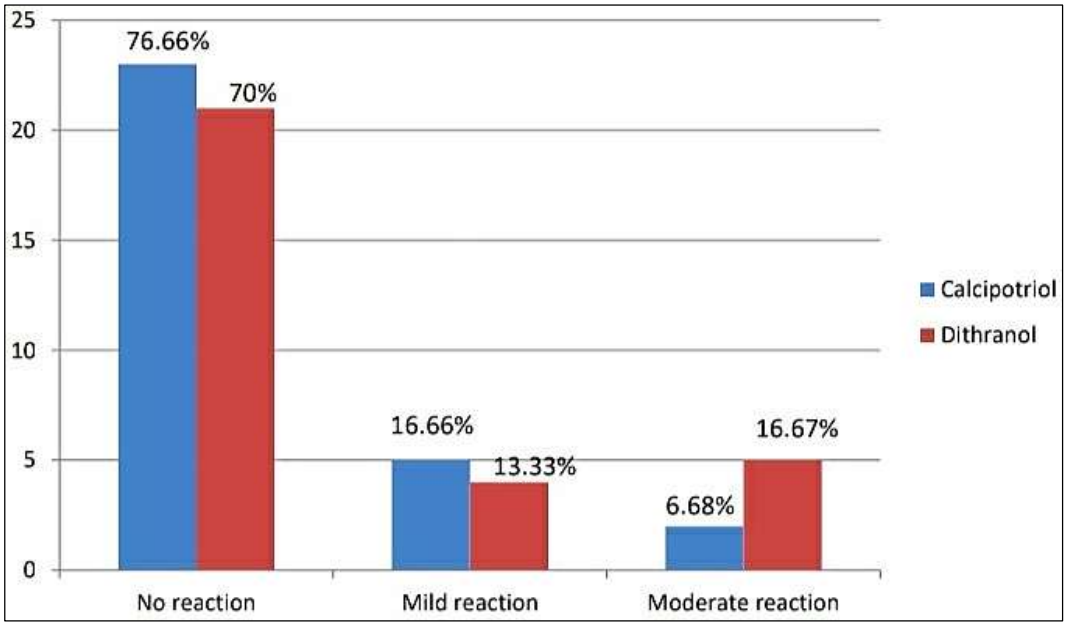


Fig 4: Clinical photo after 6 weeks of treatment with topical dithranol



Graph 2: Showing degree of cutaneous reaction

Safety

The mean score for cutaneous safety was found to be higher in dithranol group compared to calcipotriol group (0.37 vs. 0.20) when assessed by the clinician and there was no statistically significant difference between the groups (P > 0.05).

The mean score for cutaneous discomfort was found to be higher in dithranol group compared to calcipotriol group (0.47 vs. 0.30) when assessed by the subject and there was no statistically significant difference between the groups (P > 0.05) as shown in [Table 2].

On comparison of calcipotriol and dithranol groups, cutaneous reaction was absent predominantly in calcipotriol group when assessed both by the investigator (83.33% v/s 76.66%) as well as by the patient (76.66% v/s 70) as depicted in [Graph 2].

Table 2: Showing global assessment of safety and cutaneous discomfort in patients of calcipotriol group and dithranol group

	Assessed by Clinician		Assessed by Subject	
Grades	**Calcipotriol Group Number (%)**	**Dithranol Group Number (%)**	**Calcipotriol Group Number (%)**	**Dithranol Group Number (%)**
No reaction	25 (83.33)	23 (76.66)	23 (76.66)	21 (70)
Mild reaction	4 (13.33)	3 (10)	5 (16.66)	4 (13.33)
Moderate reaction	1 (3.34)	4 (13.34)	2 (6.68)	5 (16.67)

Discussion

In our study, efficacy of calcipotriol was clinically more significant than dithranol on the basis of improvement in global assessment score at week 6. Similar observations were reported by Ashcroft et al. However, they were not statistically significant.

Better improvement with calcipotriol was seen as early as 2 weeks in previous studies [4, 5, 6]. In our patient's regression of the lesions in calcipotriol group was seen by 3rd week and better efficacy was consistent.

In our study, the safety assessment score was higher in dithranol group compared to calcipotriol group as assessed clinically as well as by the subject indicating a better tolerability of calcipotriol as compared

to dithranol. But this difference was not statistically not significant. Similar findings were reported in the literature [6, 7, 8].

Calcipotriol [9, 10] binds to vitamin D receptor the vitamin D receptor is a member of the steroid receptor superfamily. It is active mainly as a heterodimer in combination with the RXR receptor Vitamin D3 derivatives also inhibit T cell proliferation in response to IL-1 and decreases T cell infiltration and keratinocyte ICAM-1 expression in treated plaques, thus exerting an immunomodulatory effect in psoriasis. These agents also exert antiangiogenic effect. In vivo, they have been shown to inhibit expression of IL-6, IL-8 and other cytokines. Also, they have been reported to reduce lymphocytes and neutrophils infiltration and to reduce expression of IL-8 and adhesion molecules (ICAM-1, ELAM-1, LFA1, VLA-3 and VLA-6).

Dithranol [11, 12, 13, 14] inhibits secretion of IL-6, IL-8 and TNF-alpha by monocytes. Dithranol can activate a prototypic form of transcription factor NF- (Kappa) B, a central transcriptional regulator of inflammation and immune responses.

The down-regulation of epidermal growth factor (EGF) receptor on epidermal cells by dithranol also may contribute to its ant psoriatic action Dithranol induces a decrease in EGF binding in a dose dependent manner.

Both calcipotriol and dithranol are effective steroid sparing agents with multimodal functions exhibiting anti-inflammatory, immunomodulatory and anti-proliferative activity.

Calcipotriol can be combined with NBUVB, acitretin and cyclosporine [15]. The advantage of this combination is reduction in dosage of oral agents and duration of phototherapy, hence ensuring better benefit risk ratio. Calcipotriol can also be employed in combination with dithranol (Minutes therapy or SCAT) for better efficacy [16]. Hence Calcipotriol ointment is valuable as a first-or second-line therapy option for the management of mild to moderate psoriasis and in combination with other anti-psoriatic agents for more severe psoriasis.

Dithranol is used in combination with NBUVB for enhanced efficacy [17].

Safety assessment

Calcipotriol has a better safety profile in comparison with dithranol with less incidence of irritation (4, 5, 6). In our study similar observations were noted with patients in dithranol group experiencing discomfort in comparison with calcipotriol group. But this finding was not found statistically significant.

Conclusions

The study was conducted to assess and compare the efficacy and safety of topical calcipotriol and topical dithranol in chronic plaque psoriasis. Calcipotriol ointment was more efficacious than dithranol ointment based on DSS and PASI scores. Calcipotriol had better safety profile in comparison with dithranol in terms of local tolerance and induced less treatment related adverse events. No adverse event in both the groups necessitated discontinuation of therapy. Dithranol, though was less efficacious than calcipotriol, it was found to be more cost effective of the two and can be considered as an alternative agent especially in treating patients belonging to low economic strata [18, 19].

References

1. Clark JM, Hana Walt PC. Inhibition of DNA replication and repair by anthralin or danthron in cultured human cells. J of Investigative Dermatol. 1982 Jul;79(1):18-2.
2. Wadhwa B, Relhan V, Goel K, Kochhar AM, Garg VK. Vitamin D and skin diseases: A review. Ind. J of Dermatol, Venereol and Leprol. 2015 Jul;81(4):344.
3. Gudjonsson JE, Elder JT. Psoriasis. In: Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffell DJ, Wolff K, editors. Fitzpatrick's Dermatology in General Medicine. 8th ed. USA: McGraw Hill.

2012;1:197-231.

4. Ashcroft DM, Po AL, Williams HC, Griffiths CE. Systematic review of comparative efficacy and tolerability of calcipotriol in treating chronic plaque psoriasis. BMJ. 2000 Apr;320(7240):963-7.
5. Berth-Jones J, Chu AC, Dodd WA, Ganpule M, Griffiths WA, Haydey RP, *et al*. A multicentre, parallel-group comparison of calcipotriol ointment and short-contact dithranol therapy in chronic plaque psoriasis. Br J Dermatol. 1992 Sep;127(3):266-71.
6. Christensen OB, Mørk NJ, Ashton R, Daniel F, Anehus S. Comparison of a treatment phase and a follow-up phase of short-contact dithranol and calcipotriol in outpatients with chronic plaque psoriasis. J of Dermatol Treatment. 1999 Jan;10(4):261-5.
7. Van Der Vleuten CJ, De Jong EM, Rulo EH, Gerritsen MJ, Van de Kerkhof PC. In-patient treatment with calcipotriol versus dithranol in refractory psoriasis. Eur. J Dermatol. 1995; 5:676-9.
8. Van de Kerkhof PC, Van der Valk PG, Swinkels OQ, Kucharekova M, De Rie MA, De Vries HJ *et al*. A comparison of twice-daily calcipotriol ointment with once-daily short-contact dithranol cream therapy: a randomized controlled trial of supervised treatment of psoriasis vulgaris in a day-care setting Br J Dermatol. 2006 Oct;155(4):800-7.
9. Milde P, Hauser U, Simon T, Mall G, Ernst V, Haussler MR *et al*. Expression of 1, 25-dihydroxyvitamin D3 receptors in normal and psoriatic skin. J of Investigative Dermatol. 1991 Aug;97(2):230-9.
10. Carlberg C. Mechanisms of nuclear signalling by vitamin D 3. In EJB Reviews. Springer, Berlin, Heidelberg, 1995, 233-243.
11. McGill A, Frank A, Emmett N, Turnbull DM, Birch-Machin MA, Reynolds NJ. The anti-psoriatic drug anthralin accumulates in keratinocyte mitochondria, dissipates mitochondrial membrane potential and induces apoptosis through a pathway dependent on respiratory competent mitochondria. The FASEB journal. 2005 Jun;19(8):1012-4.
12. Mahrle G Dithranol. Clinics in dermatology. 1997 Sep;15(5):723-37.
13. Peus D, Beyerle A, Pott M, Meves A, Pittelkow MR, Rittner H, *et al*. Anti-psoriatic drug anthralin activates JNK via lipid peroxidation: mononuclear cells are more sensitive than keratinocytes. J of investigative dermatology. 2000 Apr;114(4):688-9.
14. Mrowietz U, Jessat H, Schwarz A, Schwarz T. Anthralin (dithranol) in vitro inhibits human monocytes to secrete IL-6, IL-8 and TNF-α, but not IL-1. Br J Dermatol. 1997 Apr;136(4):542-15.
15. Calcipotriol ointment. A review of its use in the management of psoriasis Am J Clin Dermatol. 2001;2(2):95-120.
16. Monastirli A, Georgiou S, Pasmatzi E, Sakkis TH, Badavanis G, Drainas D *et al*. Calcipotriol plus short-contact dithranol: a novel topical combination therapy for chronic plaque psoriasis. Skin Pharmacology and Physiology. 2002;15(4):246-51.
17. Carrozza P, Häusermann P, Nestle FO, Burg G, Böni R. Clinical efficacy of narrow-band UVB (311 nm) combined with dithranol in psoriasis. An open pilot study Dermatology. 2000;200(1):35-39.
18. Dina Fathalla Eman, Youssef MK, Ghareb M Soliman. Liposomal and Ethosomal Gels for the Topical Delivery of Anthralin: Preparation, Comparative Evaluation and Clinical Assessment in Psoriatic Patients. Pharmaceutics. 2020;12:446.
19. Sehgal VN, Verma P, Khurana A. Anthralin/dithranol in dermatology. Int. J of Dermatol. 2014 Oct;53(10):449-60.