

Efficacy and Safety of Calcipotriol Ointment in Psoriasis Vulgaris - Experiences in Hong Kong

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ABSTRACT

Calcipotriol, a Vitamin D₃ analogue, has offered a new therapeutic approach to psoriasis. In this study of 6 week duration, we recruited 42 patients from four major skin centres of Social Hygiene Service to study the efficacy and side effects of calcipotriol ointment in chronic plaque type psoriasis. We concluded that topical calcipotriol ointment is effective in reduction of erythema, thickness and scaliness of lesions. The local irritation precludes its use in flexural and facial areas. There is no effect on calcium metabolism provided that no more than 100 gram is used per week.

Keywords: Calcipotriol ointment, psoriasis vulgaris, Hong Kong

INTRODUCTION

Psoriasis is one of the common skin diseases presented to dermatologists. It can be classified simply into either acute or chronic, pustular or non-pustular, and stable or unstable forms. The stable non-pustular form of psoriasis is the major type (up to 97%) reported in China.¹ In Hong Kong, we have similar experience as reflected by the statistical return on the number of new cases of psoriasis reported in 1996 (see Table 1). Chronic plaque type psoriasis is the commonest form

of psoriasis. It will be encountered not only by dermatologist, but by doctors of other specialties as well, such as primary care physicians and general physicians. The new effective topical treatment for this form of psoriasis is rather limited, and effective systemic treatments like methotrexate, hydroxyurea, etretinate and cyclosporin are often not given because of their potential serious long term adverse effect. Hence, a new topical therapy will certainly be welcome if it is proven to be safe and effective for this chronic recalcitrant condition. There have been new advances in the past decade in the treatment of therapy-resistant unstable psoriasis with etretinate and cyclosporin. On the other hand, treatment of stable plaque type psoriasis has remained to be a choice between emollient, salicylic acid, tar, dithranol and topical steroid preparations. These agents still have significant drawbacks in terms of unwanted side effects or cosmetic acceptability. In recent years the important role of Vitamin D in skin physiology and pathophysiology has been identified, and this offers a new therapeutic approach for psoriasis. Psoriasis is characterised by hyperproliferation and incomplete terminal differentiation of the epidermis, dilatation of capillaries in the papillary dermis and migration of activated neutrophils and T lymphocytes to both the dermis and epidermis. Receptors for calcitriol, the naturally occurring active form of Vitamin D₃, have been found in epidermal keratinocytes, dermal fibroblasts, endothelial cells and activated T lymphocytes. In cultured human keratinocytes, calcitriol

Table 1. Types of psoriasis (New Cases in Social Hygiene Service 1996)

Chronic plaque psoriasis	538	96.1%
Acute guttate psoriasis	12	2.1%
Generalised pustular psoriasis	3	0.5%
Localised pustular psoriasis	5	0.9%
Erythrodermic	2	0.4%
Total	560	

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inhibits cell proliferation and induces terminal differentiation.^{2,3} Calcipotriol, a Vitamin D₃ analogue, has the same high binding affinity to the cellular receptors for calcitriol, but has at least 100 times less effect on calcium metabolism in rats than calcitriol.⁴ When applied topically, calcipotriol has been shown to be of benefit in psoriasis as compared with placebo.⁵ The aim of this study is to assess the efficacy and safety of this drug in our local population.

METHODS

This was a multicentre, open and prospective study of calcipotriol ointment for treating chronic plaque type psoriasis in Hong Kong. Forty-two patients from both sex were recruited in four skin centres, and followed up for a treatment period of six weeks. They have mild to moderate psoriasis with less than 40% of skin surface area involved. Patients with the following characteristics were excluded: age below 16, pregnancy or inadequate contraception, known or suspected hypercalcaemia, significant systemic illness such as renal or hepatic dysfunction. They were not permitted to take any systemic antipsoriatic therapy or apply any topical treatment to the study area.

Ointment containing calcipotriol (50mg/g) was provided up to a maximal dose of 100g per week. Patients were instructed to apply it twice daily without occlusion to all affected skin areas except the face or scalp, where they could use emollient or a low potency topical corticosteroid instead.

Patients were followed up at 2 week intervals. Complete blood picture, liver function test and serum calcium level were checked at week 0 and week 6. Extent of skin lesions was assessed by simplified score from 0 to 3 (score 0: 0%; score 1: <33%; score 2: 33-66%; score 3: >66% of skin area). Severity of psoriatic lesions were recorded for three parameters: erythema, thickness and scaliness (grade 1: mild; grade 2: moderate; grade 3; severe). Both the extent and severity of lesions were assessed separately for each of the three areas: upper extremities (UL), trunk (TL), lower extremities (LL).

During each visit, the patient made their own overall assessment on the effect of calcipotriol ointment (improved, no change, or worsened). Any possible adverse events were recorded, the severity and relationship with current treatment was carefully analysed. Clinical photographs of the most severely affected region were taken at week 0 and week 6 for documentation.

RESULTS

The progression of average scores for the extent and severity of lesions in different regions over the treatment period are shown in Figure 1 to 4. Figure 5 demonstrates the patients own overall assessment of disease after using the ointment. Thirty four out of 42 patients (81%) completed the study and the drop out rate is shown in Table 2. Table 3 lists the adverse events encountered by those who have completed the study.

Table 2. Drop out rate

	Number	Reason
Premature termination	3	intolerant of adverse effect
Premature termination	2	worsening of psoriasis
Default follow up	3	unknown
Study completed	34	
Total	42	
% of drop-out	19%	

Table 3. Adverse effects (for those who completed the study)

Side effect	Number and Percentage	Severity
Local pruritis	5 (14.7%)	mild
Increase erythema	1 (2.9%)	mild
Hand dermatitis	1 (2.9%)	mild
Facial dermatitis	4 (11.8%)	mild
Percentage	11/34 (32.4%)	

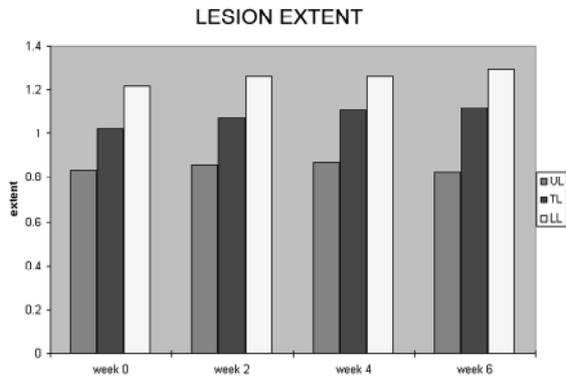


Figure 1

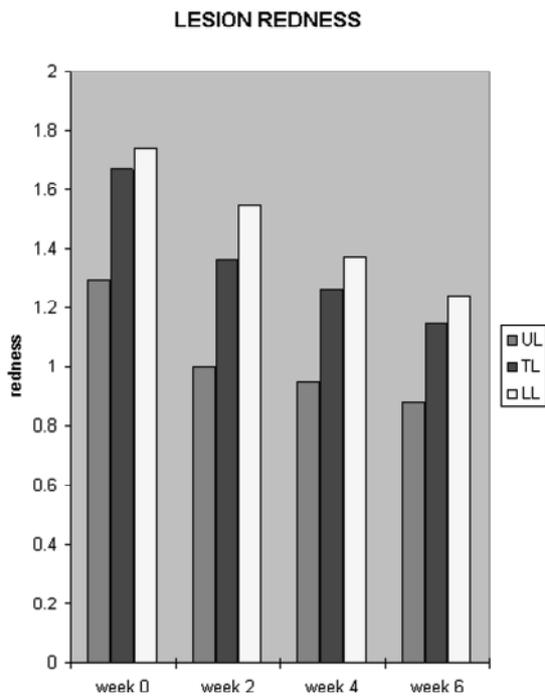


Figure 2

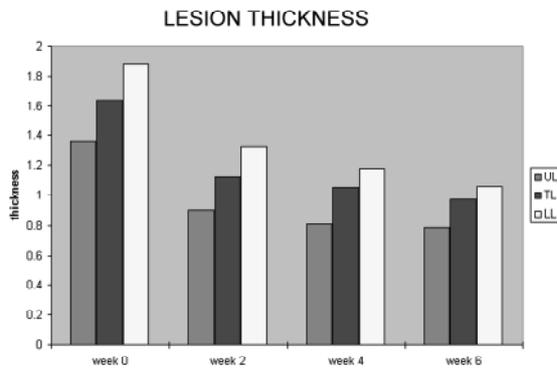


Figure 3

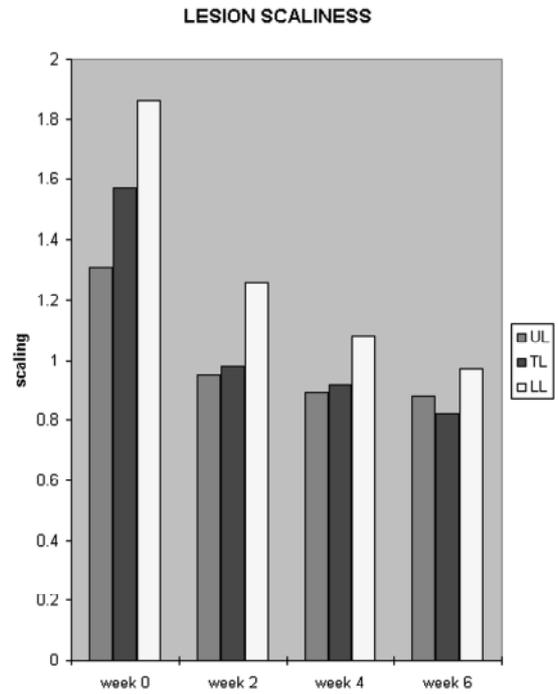


Figure 4

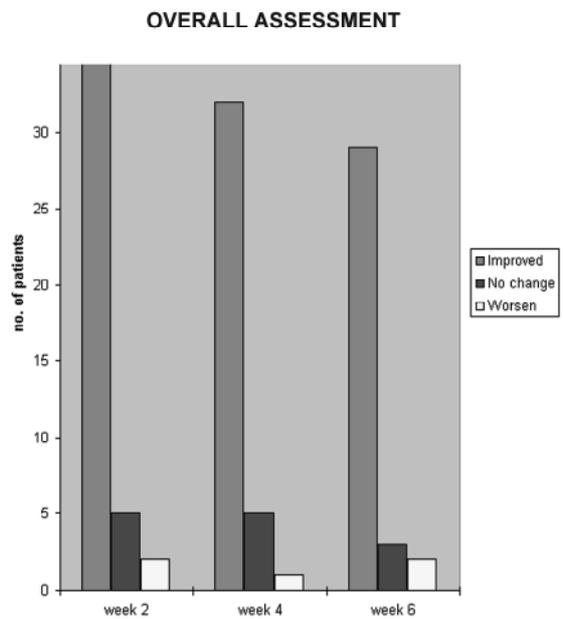


Figure 5

No biochemical abnormality had been detected in any of the patients during the treatment period.

DISCUSSION

Thirty-four out of 42 patients completed the study. Three patients requested premature termination because of burning or itchy sensation at the lesions. Two patients experienced exacerbation of psoriasis during the treatment period and the trial was stopped, even though there was no evidence attributable to calcipotriol ointment. Three others defaulted without any known reasons.

There was significant improvement in severity of lesion, namely erythema, thickness and scaliness of all areas during the 6 week treatment period. As in other studies,^{6,7} the rate of response was greatest during the first 2 weeks of treatment. However the main weakness of this study was its open design, and therefore susceptible to observer bias. There may be tendency for a new treatment to be received with more enthusiasm than other treatments previously prescribed.

On the other hand, the extent of the psoriatic lesion in all areas did not show any reduction during the treatment period. This indicates that calcipotriol ointment as a topical agent does not clear up the lesion rapidly, at least not within 6 weeks. Another possible explanation might be the scoring system in this study was too crude to reflect the subtle changes in the extent of involvement. For example, a reduction from 50% to 40% of skin area would still mean score 2 and this degree of change is not reflected in the study. Nevertheless, most of our patients do prefer the new medication as reflected by over 85% claiming improvement in their own overall assessment of the treatment. Thus although the area clearing up effect is not remarkable, our patients are satisfied with calcipotriol ointment because it improved severity of individual lesions.

The incidence of adverse events was 32.4%, all were mild and self limiting. As in other studies, local irritation and facial dermatitis predominated.^{6,7} The patients were not allowed to apply the study ointment to the face or scalp because facial irritation/dermatitis developed in some patients in a previous study.⁸ Facial dermatitis in

our patients was presumed to result from inadvertent contamination it improved after using emollients or mild corticosteroid cream. Our study also indicated that the application of up to 100gm of calcipotriol ointment (50mg/gm) per week up to six weeks carries no risk of hypercalcaemia. However, it must be stressed that monitoring the serum calcium level is a relatively insensitive method of assessing calcium metabolism and our study was only of short duration. Further studies should be carried out to evaluate the effect of long term topical calcipotriol on calcium metabolism. More sensitive parameters such as serum Vitamin D level and 24 hour urine for calcium excretion should be used in future studies.

When compared with other topical treatments for psoriasis, calcipotriol ointment is more convenient and acceptable than tar, also more effective and better tolerated than dithranol.⁹ In large, multicentre, double-blind studies of right/left comparison design, response to calcipotriol ointment was of similar order to betamethasone 17-valerate ointment (0.1%).⁶ The problem of skin atrophy with long-term topical steroid therapy was not observed clinically or in skin biopsies during calcipotriol treatment.¹⁰

In conclusion, calcipotriol ointment provides an additional therapeutic modality to the topical treatment of mild and moderate psoriasis, especially in patients who have suffered from steroid-induced skin atrophy. Its irritation precludes application on the face and flexures in some patients. The main limitations for its use as a first line agent are its cost, and its relative young age when compared with other well known topical anti-psoriatic agents.

Learning points:

Topical calcipotriol should not be applied to the face. The amount prescribed should not exceed 100 gram per week.

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