Original Article

A Comparison between Topical application of Calcipotriene, Clobetasol and a combination regime of the two drugs in the treatment of Iraqi Patients with Psoriasis Vulgaris

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Summary:

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Back ground: *Psoriasis is a chronic relapsing disorder with no life long cure, many systemic and topical modalities are available, one of these topical modalities is the vitamin D analogue (calcipotriene) which is widely used recently to treat psoriasis and many other skin problems.*
Aim of the study: *Is to compare the safety, the efficacy and the tolerability of tolerability of topical calcipotriene, topical clobetasol and both of them in combination in treating Iraqi patients with psoriasis vulgaris. (The first study in Iraq that uses calcipotriene ointment in treating psoriasis and comparing it with other known topical treatments that were commonly used to treat this problem).*
Patients and methods *A total of 128 patients with stable plaque psoriasis (72 males and 56 females) with ages between 13 and 68 years and a mean age of 36 years were included in this study, the patients put in four groups: the first one was treated with calcipotriene ointment only, the second was treated with clobetasol ointment only, the third was treated with both drugs in combination and the fourth was treated with Vaseline ointment as placebo. The patients were fully assessed clinically before, during and after the treatment.*
Results: *The study showed that the combination therapy was more effective than calcipotriene or clobetasol alone as it significantly reduced the mean percentage of PASI score within two weeks of treatment*
(in 55.9 %, 42.5% and 31.9% of the patients respectively) , the study also showed that the combination therapy had a significantly faster response and a slower relapse rate than that of each drug alone and the effect of calcipotriene appeared to be faster in patients who had no previous treatments.
Conclusion:*Calcipotriene ointment is a relatively safe, a moderately effective and a well tolerated drug, however, its combination with*
a potent (very potent) topical corticosteroid will lead to better therapeutic results than the use of each one of them alone.

Introduction:

Although Psoriasis is a chronic relapsing disease with no long life cure, a variety of treatments are available to reduce the severity of symptoms and to lessen their impact on the patients quality of life. For patients with 30% (or less) body surface involvement, topical therapy is the most appropriate choice for initial treatment, among these topical drugs are Corticosteroids, Calcipotriene (vitamin (D3) analogue), tazarotine (topical retinoid)…etc. For patients with severe, extensive or recalcitrant psoriasis, phototherapy and other systemic therapies (like methotrexate, retinoids and cyclosporine) are available, however, the use of these systemic therapies needs careful monitoring [1,2,3].

Ultimately treatment selection for each patient must take into account both the patient's disease severity and expectations for improvement, as well as the risk –- benefit ratio associated with each potential therapy. Vitamin D3 analogues have revolutionized the topical treatment of psoriasis during the last decade. The mode of action of this ligand for vitamin D3 receptor is via modulation of the transcription of genes with vitamin D3 response elements in the promoter region. Vitamin D3 analogues cause inhibition of various aspects of cutaneous inflammation and epidermal proliferation with enhancement of normal keratinization and promotion of differentiation.[4,5,6] Topical corticosteroids as a monotherapy or in combination with other drugs were widely used in the management of patients with psoriasis but not without adverse effects.[7,8].Recently, Calcipotriene has been available as a routine treatment in Iraqi hospitals.

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Patients and methods:
One hundred twenty eight patients with stable plaque type psoriasis (psoriasis Vulgaris) were enrolled in this single – blind, controlled, parallel

group study which was conducted in the out-patient clinic of the Department of Dermatology and Venereology of the teaching hospital of Al-Kadhymia in the period from July 2000 to April 2001. They were 72 males and 56 females with ages ranged from 13 to 68 years with a mean age of 36 years, the age of onset was between 13 and 63 years with a mean of 31.8 years.

The patients were divided into 4 groups:

⇒ Group 1 (34 patients), applied topical 0.005 % Calcipotriene ointment (Daivonex) [manufactured by LEO pharmaceutical Products Company] twice daily as a monotherapy.

⇒ Group 2 (30 patients), applied topical 0.05 % Clobetasol dipropionate ointment (Dermodin) [manufactured by the Iraqi pharmaceutical Products Company of Samarra] twice daily as a monotherapy too.

⇒ Group 3 (30 patients), applied topical 0.005 % Calcipotriene ointment (of the same previously mentioned company) in the morning and topical 0.05 % Clobetasol dipropionate ointment (of the same previously mentioned company) in the evening (or at night).

⇒ Group 4 (34 patients), this control group used white soft paraffin (Vaseline ointment) {manufactured by Syrian company} twice daily.

The treatment was continued for 6 weeks (till the clearance of the lesions occurred), after which patients discontinued treatment. An evaluation of the over all treated lesions was performed at each follow up visit, during the treatment period and for another 8 weeks after discontinuation of treatment. All patients were told to come for assessment at weekly intervals during the treatment period and bimonthly(every two weeks) intervals for the follow up period.

i-Assessment:

Assessment was performed initially at the beginning of treatment (week 0), and on week 1, week 2, week 3, week 4, week 5 and week 6, knowing that the treatment continued till clearance of the lesions achieved. Also patients were reassessed clinically at 2 weeks intervals after clearance(for 8 weeks) to determine the rate of relapse within each group. Assessment of all patients was recorded using the PASI score: (Psoriasis Area and Severity Index) which is calculated from the following formula[9]:

$$\frac{0.3A(TES)}{\text{Trunk}} + \frac{0.4A(TES)}{\text{Lower Limbs}} + \frac{0.2A(TES)}{\text{Upper Limbs}}$$

Where T= Thickness, E= Erythema and S= Scaliness, this TES had from 0 ——— 4 score.

The same observer performed the assessment at each visit, all patients subjected to the study received no previous systemic treatment and had 30 % (or less) body psoriasis. The relapse for each group was assessed when new lesions involved 50% or more of the surface area initially affected before the treatment was established.

ii-Statistical analysis:

An expert statistical advice was sought for. Statistical analyses were done using SPSS version 7.5 computer software (statistical package for social sciences). The statistical significance of difference in response (or relapse) rate between the three study groups was assessed by Chi – square test [(P value < 0.05) was considered as a statistically significant result]. The statistical significance of the differences in mean percent reduction in PASI between the three study groups was assessed by ANOVA test[10].

Results:

Analysis of data obtained showed the following results:

For the group receiving a combined therapy, 6 (20%) of them showed an effective response after two weeks and a maximum response rate for this group was seen after four weeks of treatment while 2 (6.7%) of the Clobetasol group patients showed an effective response after two weeks with a maximum response rate seen after five weeks of treatment and 2 (5.9%) of the Calcipotriene group patients showed an effective response after three weeks with a maximum response rate reached after six weeks of treatment. (Fig. 1)

The mean percent reduction in PASI score for the group receiving the combined therapy was significantly higher (55.9%) after two weeks of therapy than in those receiving Clobetasol alone (42.5%) which in turn was higher than the mean percent reduction for the Calcipotriene group (31.9%). (Fig. 2)

The combination group showed a significantly slower rate of relapse (at each of the four bimonthly intervals of follow up) when compared to the Calcipotriene group which in turn is with a slower relapse rate than the group receiving Clobetasol alone. (Fig. 3).

The patients who were treated for the first time (never treated before) [14 (41.2%) of the first group patients] had a better and faster response to Calcipotriene than those who were treated before, however, skin irritation developed in 9(26.4%) of the patients who were treated with Calcipotriene alone , all other patients developed no side effects. Treatment with Vaseline had no significant effects on psoriatic lesions .Age and sex of the patients had no major effect on the response to therapy.

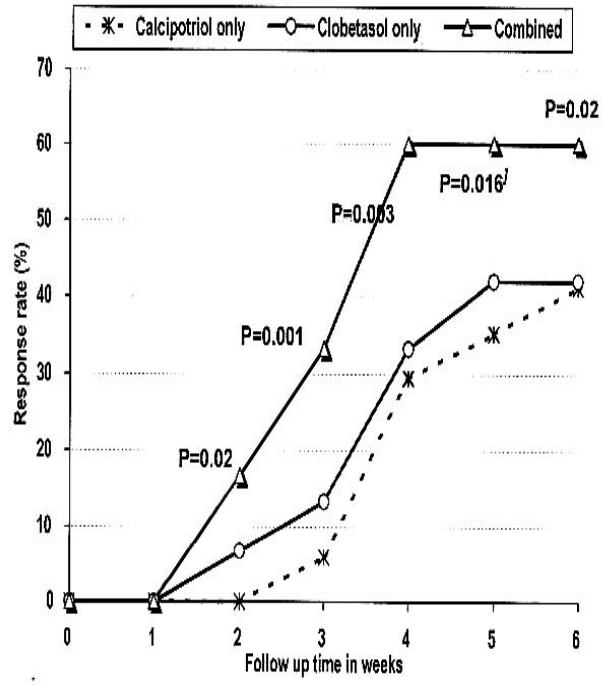

Fig. 1: Line diagram showing the time trend and the differences in response rate between the three study groups at each of the 6 weeks intervals of follow up

Note: P value was assessed by Chi – square test.

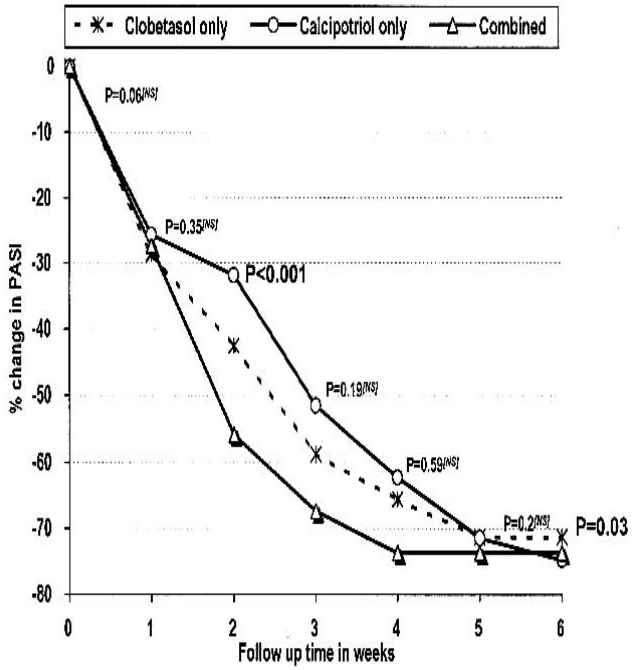

Fig. 2: Line diagram showing the time trend and the differences in mean percent reduction in PASI score (compared to its baseline value) between the three study groups at each of the 6 weeks intervals of follow up

Note: P value was assessed by ANOVA

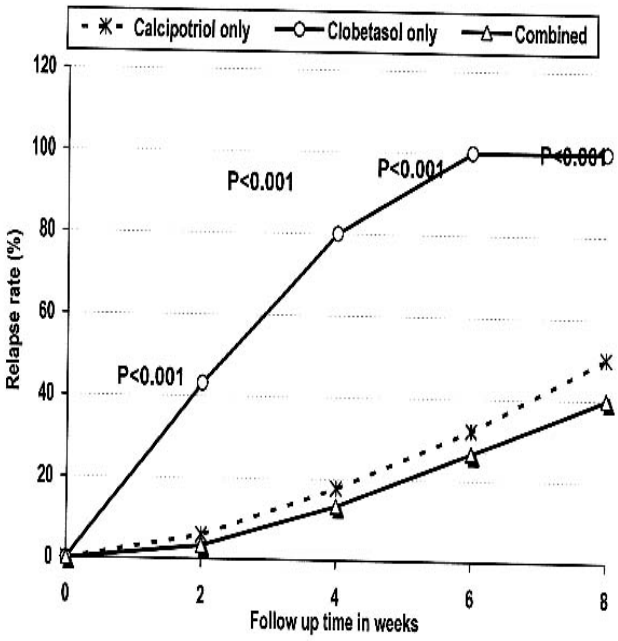

Fig. 3: Line diagram showing the time trend and the differences in relapse rate between the three study groups at each of the post treatment bimonthly interval of follow up

Note: P value was assessed by Chi – square test.

Discussion:

Topical corticosteroids are commonly prescribed for the treatment of psoriasis around the world, unfortunately, the use of topical corticosteroids is usually with several side effects especially if the very potent types are used. Since psoriasis is a chronic disease and usually requires prolonged therapy, regimes had developed to minimize the side effects of treatment.[5] One of the most widely used regime involves the application of a very potent steroid (class I) until flattening of the plaque occurs, thereafter, the steroid is applied on weeks ends only (weekend or pulse therapy) and this had the advantage of prolonging psoriasis remission while avoiding the cutaneous atrophy and the other side effects, however, many patients complain of early relapse if they are not received their daily steroid dose. [8] Calcipotriene has been recently introduced in Iraq for the treatment of psoriasis. Several studies abroad have compared it favorably to mid potency steroids. [6,7], and as seen in this study, the very potent steroids are superior to Calcipotriene in short- term studies. [7]. Our study also showed that the Calcipotriene / Clobetasol combination regime resulted in an effective response after two weeks reaching a maximum rate response after four weeks of treatment and this result goes in accordance with other studies [5].The mean percent

reduction in PASI score was significantly higher for the combined group when compared to its baseline value at the end of two weeks therapy than the other two groups while the reduction in the Clobetasol group is higher than the Calcipotriene group and this result is consistent with the literature. [7.]

The relapse rate was shown to be slowest in the combined regime group followed by the Calcipotriene group which in turn was with slower rate than the Clobetasol group and this result is also seen in other studies. [5,6], however, the faster response of Calcipotriene in those who are not treated before was not mentioned in other studies.

Conclusion:

Calcipotriene ointment is a relatively safe, a moderately effective and a well tolerated drug, however, the greatest use of it may come from a long term combination with topical steroids, also this combination can abolish the cutaneous irritation which follow the use of Calcipotriene.

Studies are currently under way in which Calcipotriene is applied on week days and class I steroid on week ends. In combining Calcipotriene with other agents it should be stressed that both medications should be applied at different times. If Calcipotriene is mixed with other agents, the two must be proven to be compatible because Calcipotriene is easily inactivated [11].

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