

Improvement of health-related quality of life and adherence to treatment with calcipotriol-betamethasone dipropionate gel in patients with psoriasis vulgaris*

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Abstract: BACKGROUND: Psoriasis is a common, chronic, recurrent, immune-mediated disorder of the skin and joints. It can have a significant negative impact on the physical, emotional and psychosocial wellbeing of affected patients.

OBJECTIVES: To measure improvement in health-related QoL (HRQoL) in Greek patients with psoriasis vulgaris after a month of treatment with calcipotriol-betamethasone dipropionate gel; and evaluate adherence to treatment parameters.

METHODS: The study included 394 psoriasis vulgaris patients from 16 private dermatological practices in Greece, all treated with calcipotriol-betamethasone dipropionate gel. They were evaluated at the first visit and after 4 weeks. Moreover, they completed the Dermatology Life Quality Index (DLQI), while other data such as disease severity, subjective symptoms and adherence, were collected.

RESULTS: At week 4, the DLQI median was reduced by 3.5 points from the baseline ($p < 0.001$; baseline and week 4 median: 4.5 and 1.0 respectively). Pruritus and sleep disorders also improved ($p < 0.001$). Furthermore, 90.1% of the subjects fully adhered to treatment, with a 97.1% mean level of compliance.

CONCLUSIONS: The convincing clinical results, with a distinct improvement in HRQoL, plus the high level of adherence due to its advantageous physical properties, make the calcipotriol-betamethasone dipropionate gel formulation an important, effective and well-tolerated topical therapy to treat psoriasis.

Keywords: Indicators of quality of life; Psoriasis; Quality of life

INTRODUCTION

Psoriasis is a common autoimmune disease entailing cutaneous inflammation and keratinocyte hyperproliferation with a complex immunogenetic basis.¹ The natural history of the disorder is usually chronic and typically follows a relapsing and remitting course.² The most common form of psoriasis is psoriasis vulgaris (~80%-90% of psoriatic patients), defined by well-delineated, red, scaly plaques that typically affect the elbows, knees, scalp and intergluteal cleft.¹ In a recent systematic review, the prevalence was found to vary from 0% (Taiwan) to 2.1% (Italy), and between 0.91% (United States) and 8.5% (Norway), in children and adults respectively.² In an 8-year epidemiological study (1995-2002), plaque psoriasis prevalence in a

Greek outpatient setting was estimated at 2.8%.³

Psoriasis has a profound, multidimensional impact on patients' quality of life (QoL). Traditionally, the physical burden entails disease symptoms, such as pruritus, scaling, burning and dry skin, and/or pain; it can also impair patients' physical functioning, sleep and leisure.⁴⁻⁸ Furthermore, psoriasis is associated with significant psychological morbidity, through considerable anxiety, depression, loss of behavioral or emotional control and psychological well-being, in addition to a wide range of emotional reactions, including shame, embarrassment, self-consciousness, anger, frustration, helplessness and body cathexis problems.⁹⁻¹¹ The physical and psychosocial aspects of psoriasis are interre-

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lated, leading to a vicious circle, where the physical and mental elements of health interact in a progressively negative way, resulting in the worsening of the condition in most patients.¹²

Due to the chronic nature of the disease, treatment aims to mitigate the physical symptoms and improve patients' QoL. Calcipotriol-betamethasone dipropionate is a fixed-dose combination of a vitamin D₃ analogue and a corticosteroid, indicated for the once daily, topical treatment of psoriasis vulgaris of the trunk, limbs, and scalp in adults. It has been developed as an ointment and a gel formulation,¹³ while its efficacy and safety in treating psoriasis vulgaris of the trunk and/or limbs has been evaluated in ten randomized, clinical trials, involving over 7,000 subjects.¹⁴ Five randomized clinical trials have assessed the treatment of psoriasis vulgaris of the scalp, comprising more than 3,000 patients.¹⁴ The two-compound therapy proved more effective and better tolerated than both placebo, calcipotriol and tacalcitol monotherapies. In most instances, it also proved more effective than betamethasone, and was at least as well-tolerated.

To date, little information has been published on the impact of psoriasis on the QoL of Greek subjects. Most studies have examined the nail involvement of psoriasis and epidemiological issues, while few interventional studies have investigated QoL aspects. Moreover, the efficacy of calcipotriol-betamethasone dipropionate therapy, as well as its impact on QoL, remain to be evaluated.¹⁵⁻¹⁸ In addition, to the best of our knowledge, treatment adherence concerning any first-line topical treatment has not been previously assessed in Greece. Compliance with topical treatment in psoriasis is generally deficient, due to: difficulties in self-application, poor cosmetic characteristics in the vehicle used, the frequency of applications and side effects (or even fear of side effects), as well as low efficacy of prescribed medicines.^{19,20}

The primary objective of the ORACLE study was to measure improvement in health-related QoL (HRQoL) in Greek patients with psoriasis vulgaris after a month of treatment with calcipotriol-betamethasone dipropionate gel, and to evaluate adherence to treatment parameters with a multicenter, open-label, prospective study design.

MATERIALS AND METHODS

Patients and study design

A multicenter (16 private dermatological practices in Greece), open-label, prospective study of Greek psoriasis patients was conducted between December 2012 and March 2013. The survey included all subjects diagnosed with mild to moderate psoriasis vulgaris localized in the scalp, upper/lower extremities and main body; and who were due to initiate treat-

ment with calcipotriol-betamethasone dipropionate gel under routine clinical practice (once daily regimen). However, it excluded patients who: were unable to complete the questionnaire themselves, were aged above 18 or had participated in another clinical study during the preceding 3 months. All patients gave their informed consent and the survey was conducted in accordance with the Declaration of Helsinki.

The study design allowed for two visits, with a period of 4 weeks between them. At the first visit, information was gathered on socio-demographics, clinical characteristics, concomitant conditions, and generic (EQ-5D) and dermatology-specific HRQoL; while subjective pruritus symptoms and sleep disorders were also measured.^{21,22} During the second visit, we collected data on adherence to treatment parameters, applied the Patient Global Impression of Change (PGIC) scale regarding patients' conditions and changes in dermatology-specific HRQoL, and recorded subjective symptom ratings.

Assessments

The dermatology-specific HRQoL was measured using the Dermatology Life Quality Index (DLQI). It is a 10-item instrument designed for a wide range of dermatological conditions,²³ covering: symptoms and feelings (items 1 and 2), daily activities (items 3 and 4), leisure (items 5 and 6), work and school (item 7), personal relationships (items 8 and 9) and treatment (item 10).²⁴ Patients respond on a 4-point scale, with higher scores representing greater impairment in QoL, based on their experiences over the preceding 7 days. The total DLQI score represents the sum of the scores for each question, and can be expressed as a number from 0 to 30.²⁴ Further, patients can be classified into 5 groups according to their total DLQI score. Psoriasis may have: 1) no effect (0-1), 2) little effect (2-5), 3) a moderate effect (6-10), 4) a very large effect (11-20), or 5) an extremely large effect, on patients' lives (21-30).²⁴ The study's primary endpoint was the mean improvement in DLQI scores between the baseline and week 4.

Secondary endpoints concerned disease severity. The Psoriasis Global Assessment (PGA) scale was used to evaluate clinical severity.²⁵ The investigator assigned a single estimate of the patient's overall disease severity, drawing on a 3-point scale, i.e. mild, moderate and severe psoriasis, measuring the physician's assessment of the disease at a given moment (static form).²⁵ Furthermore, patients subjectively rated their psoriasis-related symptoms of pruritus and sleep disorders on scales ranging from 1 (no itching/sleep problems) to 10 (worst possible state). PGIC was measured on a 7-point scale (much better, better, a little better, no change, a little worse, worse, much worse).

At the second visit, the attending physician provided information on the subject's treatment adherence during the previous 4 weeks. Physicians were asked whether the patient fully complied with the medical guidelines, the reasons for compliance or non-compliance, respectively, as well as the number of days on which the patient received less of the prescribed doses, or none at all. They also rated the total compliance level on a scale from 0% (absence of compliance) to 100% (full compliance). Treatment safety was investigated by monitoring serious adverse events reported by patients.

Analysis

Descriptive statistics (mean/standard deviation, frequency, proportion, median, interquartile) of the demographic and clinical characteristics are reported. Changes in DLQI scores and clinical measurements at week 4 were evaluated using the non-parametric Wilcoxon Signed Ranks test, while proportion changes in median scores were also estimated. All comparisons were evaluated on the 5% level of statistical significance. Descriptive statistics were employed to explore adherence to treatment. Statistical analysis was carried out using the IBM SPSS Statistics 21 software package.

RESULTS

Patients

Of the 396 subjects enrolled in the study, 394 (99.49%) completed the 4-week study period; there was one withdrawal and one subject was lost to follow-up. Baseline patient demographics and disease characteristics are displayed in table 1. The mean generic HRQoL value was estimated at 0.73 (SD 0.25) and 0.74 (0.23) by the EQ-5D-3L and EQ-5D-5L instruments respectively, while patients had a mean health state of 74.7 (SD 18.1), according to the VAS scale.

Improvement of dermatology-specific QoL

Wilcoxon Signed Ranks tests demonstrated a statistically significant ($p < 0.001$) decrease in all DLQI scores after 4 weeks of treatment, meaning that dermatology-specific HRQoL improved in all related aspects (Table 2). In particular, the DLQI summary median score decreased from 4.5 at the baseline to 1.0 after 4 weeks of therapy, which represents a 77.78% reduction. The median dimension scores for symptoms and feelings, as well as daily activities, decreased by 50% and 100%, respectively, while all dimension scores underwent a reduction in their 3rd quartile from 1 to 2 points. These changes translate into an increased proportion of patients (from 16.46% to 58.93%) on whom psoriasis had no effect (Graph 1).

TABLE 1: Baseline demographics and clinical characteristics

	N (%)
Gender	
Males	238 (60.1)
Females	158 (39.9)
Age	
18-24	13 (3.3)
25-34	62 (15.7)
35-44	71 (17.9)
45-54	60 (15.2)
55-64	75 (18.9)
65+	115 (29.0)
Educational level	
Not attended	3 (0.8)
Primary school	83 (21.0)
Lower secondary	67 (17.0)
Higher secondary	106 (26.8)
University	136 (34.4)
BMI(kg/m²)	
Underweight to normal	132 (36.7)
Overweight	147 (40.8)
Obese	81 (22.5)
Smoker	
No	264 (66.7)
Yes	132 (33.3)
Heredity	
1 st degree relative	95 (24.0)
2 nd degree relative	55 (13.9)
	Median (IQR)
Age	53.1 (28.4)
BMI(kg/m²)	26.6 (5.3)
Age at onset of psoriasis	36.6 (22.6)
Years with symptoms	8.7 (18.5)
Number of flares over the past year	3.0 (2.0)
Flare average length (days)	20.0 (20.0)
	Mean (SD)
EQ-5D-3L index	0.73 (0.25)
EQ-5D-5L index	0.74 (0.23)
VAS	74.7 (18.1)

SD: Standard deviation; BMI: Body Mass Index; VAS: Visual Analogue Scale

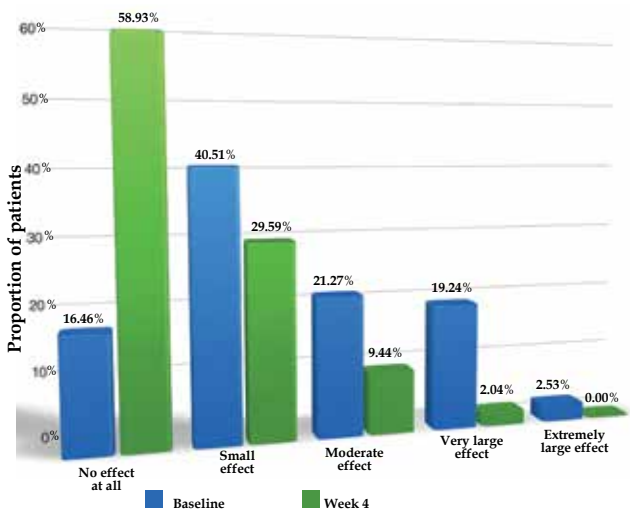
Disease severity

Physicians' ratings of patients' disease severity decreased at week 4, as the proportion of subjects with mild severity increased from 34.60% to 69.21% (Graph 2). Moreover, at follow-up, 97.46% of patients considered that their condition had improved at least a little (Graph 3). In particular, 40.97% of subjects reported being much better, 36.64% better and 19.85% a little better. At follow-up, significantly lower mean scores for pruritus and

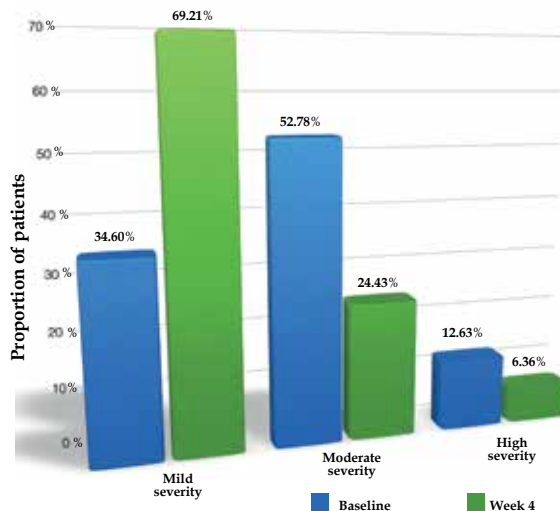
TABLE 2: Changes in dermatology-specific QoL between baseline and week 4 (n=394)

	Baseline			Week 4			Wilcoxon Signed Ranks test p-value	Change in median (%)
	Median (IQR)	Q1	Q3	Median (IQR)	Q1	Q3		
DLQI sum score	4.5 (8.0)	2	10	1.0 (3.0)	0	3	<0.001	-77.78
Dimension score: Symptoms and feelings	2 (2)	2	4	1 (2)	0	2	<0.001	-50.00
Itchy, sore, painful or stinging	1 (1)	1	2	0 (1)	0	1	<0.001	-100.00
Embarrassed or self-conscious	1 (1)	1	2	0 (1)	0	1	<0.001	-100.00
Dimension score: Daily activities	1 (2)	0	2	0 (0)	0	0	<0.001	-100.00
Shopping, looking after home or garden	0 (1)	0	1	0 (0)	0	0	<0.001	-
Influenced the clothes wearing	0 (1)	0	1	0 (0)	0	0	<0.001	-
Dimension score: Leisure	0 (1)	0	1	0 (0)	0	0	<0.001	-
Affected social or leisure activities	0 (1)	0	1	0 (0)	0	0	<0.001	-
Difficulty playing sports	0 (0)	0	0	0 (0)	0	0	<0.001	-
Dimension score: Work and school	0 (1)	0	1	0 (0)	0	0	<0.001	-
Dimension score: Personal relationships	0 (2)	0	2	0 (0)	0	0	<0.001	-
Partner-Close friends-Relatives	0 (1)	0	1	0 (0)	0	0	<0.001	-
Sexual problems	0 (1)	0	1	0 (0)	0	0	<0.001	-
Dimension score: Treatment	0 (1)	0	1	0 (0)	0	0	<0.001	-

IQR: Interquartile range; Q1:1st quartile; Q3:3rd quartile; DLQI: Dermatology Life Quality Index



GRAPH 1: Impact of psoriasis on dermatology-specific quality of life at baseline and at week 4 (n=394)



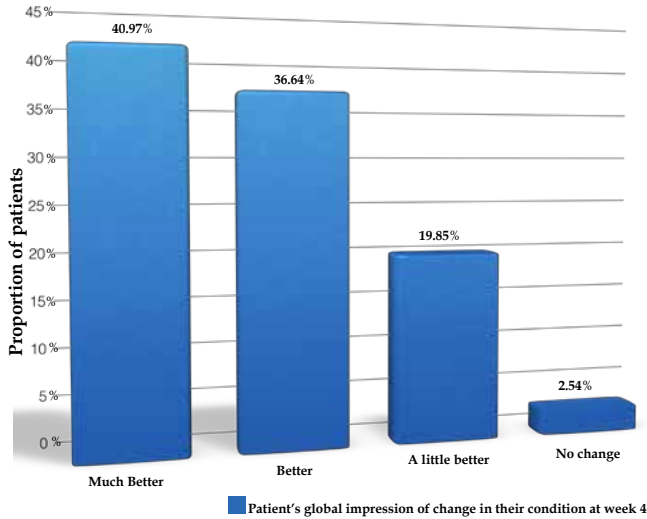
GRAPH 2: Disease severity at baseline and at week 4 (n=393)

sleep disorders ($p < 0.001$) were recorded, indicating milder also psoriasis-related subjective symptoms (Graph 4).

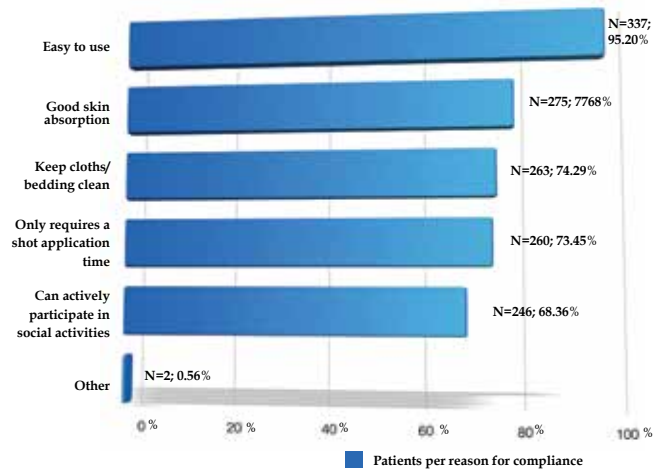
Adherence to treatment

Results revealed that 90.1% of subjects (n=355) fully adhered to treatment. Out of 6 patients (1.52%) who discontinued treatment: 1 fully remitted after ten days, 2 were concerned about possible adverse effects, 1 forgot, 1 decided to manage the disease without treatment, while another did not have the financial means. In cases of non-full compliance, 5.32 (SD 5.92) and 4.28 (SD 2.14) were the respective mean numbers

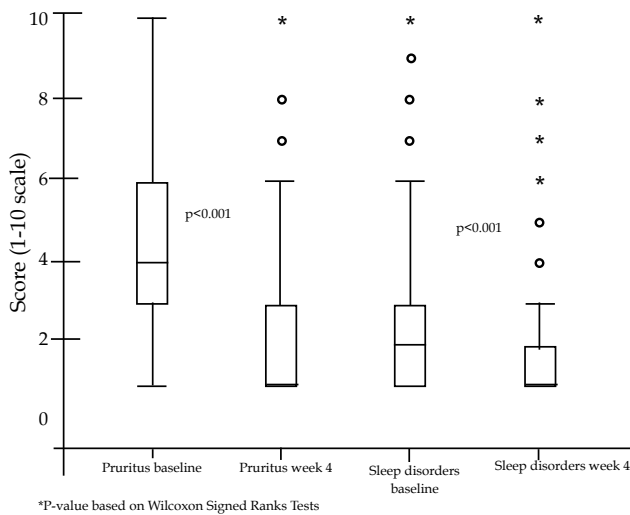
of days during which subjects received less of the prescribed doses, or none at all. Physicians estimated the mean compliance level to be 97.1% (SD 10%). Among subjects who fully complied, the main reasons mentioned for compliance with the two-compound treatment were: easy use (n=337; 95.20%), good skin absorption (n=275; 77.68%), good cosmetic characteristics of the vehicle (n=263; 74.29%), short consumption time (n=260; 73.45%) and little interference in social activities (n=246; 68.36%) (Graph 5). Meanwhile, patients who did not fully comply cited forgetfulness (n=26; 68.42%) and disregard for the importance of adherence



GRAPH 3: Patient's global impression of change in their condition at week 4



GRAPH 5: Patients per reason for compliance (n=354)

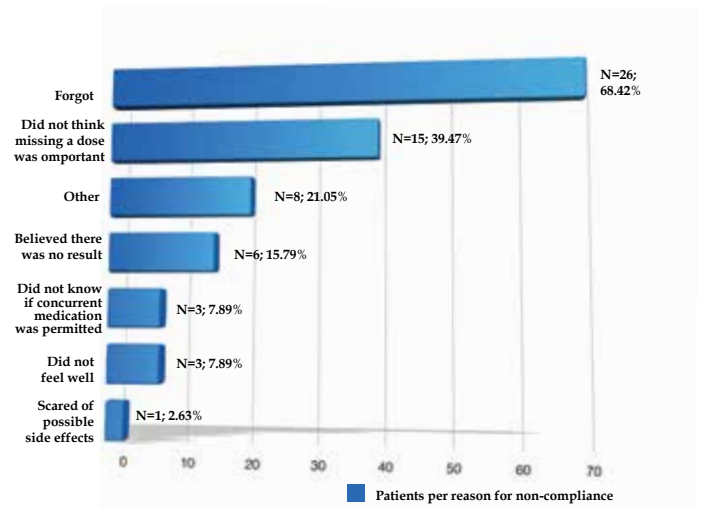


GRAPH 4: Changes in psoriasis-related subjective symptoms of pruritus and sleep disorders at week 4 (n=393)

to treatment (n=15; 39.47%) as the main explanations for non-compliance. Only 6 patients reported possible low efficacy, 3 stated they did not feel well, 3 subjects feared concurrent medication implications, while 1 was concerned about possible side effects (Graph 6).

Safety

No serious adverse events occurred during the 4-week study period. Mild adverse events such as itching and erythema occurred in some patients (less than 10) but did not discourage them from continuing treatment.



GRAPH 6: Patients per reason for non-compliance (n=38)

DISCUSSION

The two-compound treatment substantially improved all dermatology-related aspects of HRQoL (p<0.001), measured using the DLQI. At the end of the study, 58.93% of subjects were free of any HRQoL impact by psoriasis. Previous studies have also shown that the fixed combination of once or twice daily treatment improves the QoL of patients with body psoriasis significantly more than placebo, calcipotriol twice daily (only the once daily regimen). No significant differences were found between calcipotriol-betamethasone dipropionate once daily and clobetasol propionate spray twice daily.²⁶ Similarly, the two-compound gel formulation was more effective than calcipotriol solution at improving HRQoL in subjects suffering from scalp psoriasis.²⁷ In this study, the difference in DLQI summary scores between the baseline and week

4 was smaller than previously found, probably owing to the lower baseline scores.²⁸ Nevertheless, this difference was within the range of the Minimal Important Difference of DLQI for psoriasis (2.3-5.7), constituting a meaningful change in HRQoL.²⁹

Changes in disease severity and symptoms were also examined. The results were similar to those of all previous randomized clinical trials, where the efficacy of the two-compound therapy was well-established. A proportion of 69.21% of the subjects were classified by their physicians as suffering from mild psoriasis at week 4, compared with the 34.60% at the baseline. However, the 3-point PGA scale used was not so sensitive to changes, as self-assessments revealed that 97.46% of the patients considered their condition had improved at least a little at follow-up. Furthermore, since psoriasis is a highly symptomatic, chronic disorder, limiting the impact of its symptoms is crucial in managing the disease. Some symptoms (itchiness, soreness, pain, stinging) are covered by the DLQI questionnaire. However, we further investigated changes in the subjective symptoms of pruritus and sleep disorders. Again, a significant amelioration was recorded in both measures at week 4 ($p < 0.001$).

The two-compound regimen was well-tolerated, with only 1.5% of the subjects discontinuing treatment. None of the discontinuations was attributed to adverse effects. In earlier studies, only 0.6-2.8% of patients withdrew due to intolerable adverse events, which compares favorably with the results in the monotherapies groups.³⁰⁻³² In the previous 4-8 week clinical trial of the two-compound gel or ointment once or twice daily formulations, most adverse treatment reactions were lesional or perilesional effects of mild or moderate severity, affecting 2.9-10.9% of treated subjects. In particular, the incidence of mild effects from the gel formulation ranged between 3.4-8.8%, often with fewer lesional/perilesional adverse reactions than monotherapies.^{31,32} Although safety was not the main focus of this study, no serious adverse events occurred during the study period. Overall, only one serious adverse event (facial oedema) - possibly related to one of the two-compound formulations - has been observed so far (ointment vehicle).³³

Studies evaluating patient-reported outcomes in routine clinical practice may yield different results from those in clinical trials where patient populations are generally more homogenous.³⁴ In daily practice, efficacy and safety are not the only factors that influence the use of, and adherence to, a therapy. Other factors, such as tolerability, cosmetic characteristics, ease of use and economic burden, determine compliance and therefore clinical outcomes.^{35,36} Improvements in compliance increase treatment efficacy; thus, the topical agent's characteristics and quality are crucial in managing psoriasis.³⁷

The frequency of applications varies between 50% and 60% of expected levels as per prescription in real-life settings; and between 55% and 100% in randomized controlled trials, while patients apply between 35% and 72% of the recommended dose. In this study, the vast majority of subjects (90.1%) fully adhered to the two-compound gel formulation regimen, while the sample had a very high mean level of compliance (97.1%). Although the study did not directly assess satisfaction, subjects acknowledged the medication's good cosmetic characteristics, the short consumption time required and convenience of use. Furthermore, low adherence was associated mainly with negligence, and less with frustration related to therapy efficacy expectations or fear of side effects. Meanwhile, inconvenience was not reported as an issue. This implies that treatment with the two-compound gel formulation is characterized by a higher adherence level than the other topical therapies in daily practice.

In addition to the choice of medication, the vehicle used and patients' acceptance of treatment also affect the medication's efficacy. Both the gel and ointment two-compound formulations have proven to be efficient treatments in managing psoriasis, but they have not hitherto been tested head-to-head. In a real-life, non-interventional study, approximately 75% of the patients were satisfied or very satisfied after one calcipotriol-betamethasone dipropionate ointment treatment course, regardless of initial disease severity.^{26,31} The gains patients draw from the galenic form of the two-compound regimen, as compared to their prior treatment, has also been documented.³⁸ A cost-effectiveness study has shown that using the gel formulation, rather than the ointment form, allows a 5% reduction in the number of patients who might otherwise be treated with more expensive therapies, consequently lowering total annual treatment costs.³⁹

This can be explained by higher adherence to treatment due to the gel vehicle, which may be a more cosmetically acceptable formulation for use on body psoriasis than the ointment.³⁹

CONCLUSIONS

Convincing clinical results, including a distinct improvement in HRQoL, and the higher level of adherence linked to its advantageous physical properties, make calcipotriol-betamethasone dipropionate gel formulation an important, effective and well-tolerated topical therapy for the symptomatic treatment and management of psoriasis. □

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REFERENCES

1. Lebowhl M. Psoriasis. *Lancet*. 2003;361:1197-204.
2. Parisi R, Symmons DP, Griffiths CE, Ashcroft DM; Identification and Management of Psoriasis and Associated Comorbidity (IMPACT) project team. Global epidemiology of psoriasis: a systematic review of incidence and prevalence. *J Invest Dermatol*. 2013;133:377-85.
3. Kyriakis KP, Palamaras I, Pagana G, Terzoudi S, Evangelou G. Lifetime prevalence fluctuations of chronic plaque psoriasis and other non-pustular clinical variants. *J Eur Acad Dermatol Venereol*. 2008;22:1513-4.
4. Ljosaa TM, Mork C, Stubhaug A, Moum T, Wahl AK. Skin pain and skin discomfort is associated with quality of life in patients with psoriasis. *J Eur Acad Dermatol Venereol*. 2012;26:29-35.
5. Reich A, Hrehorow E, Szepletowski JC. Pruritus is an important factor negatively influencing the well-being of psoriatic patients. *Acta Derm Venereol*. 2010;90:257-63.
6. Finlay AY, Coles EC. The effect of severe psoriasis on the quality of life of 369 patients. *Br J Dermatol*. 1995;132:236-44.
7. Gupta MA, Gupta AK. Age and gender differences in the impact of psoriasis on quality of life. *Int J Dermatol*. 1995;34:700-3.
8. Shutty BG, West C, Huang KE, Landis E, Dabade T, Browder B, et al. Sleep disturbances in psoriasis. *Dermatol Online J*. 2013;19:1.
9. Nichol MB, Margolies JE, Lippa E, Rowe M, Quell J. The application of multiple quality-of-life instruments in individuals with mild-to-moderate psoriasis. *Pharmacoeconomics*. 1996;10:644-53.
10. Devrimci-Ozguven H, Kundakci TN, Kumbasar H, Boyvat A. The depression, anxiety, life satisfaction and affective expression levels in psoriasis patients. *J Eur Acad Dermatol Venereol*. 2000;14:267-71.
11. Rakhesh SV, D'Souza M, Sahai A. Quality of life in psoriasis: a study from south India. *Indian J Dermatol Venereol Leprol*. 2008;74:600-6.
12. Tabolli S, Naldi L, Pagliarello C, Sampogna F, di Pietro C, Spagnoli A, et al. Evaluation of the impact of writing exercises interventions on quality of life in patients with psoriasis undergoing systemic treatments. *Br J Dermatol*. 2012;167:1254-64.
13. Papp KA, Guenther L, Boyden B, Larsen FG, Harvima RJ, Guilhous JJ, et al. Early onset of action and efficacy of a combination of calcipotriene and betamethasone dipropionate in the treatment of psoriasis. *J Am Acad Dermatol*. 2003;48:48-54.
14. Girolomoni G, Vena GA, Ayala F, Cannavò SP, De Pittà O, Chimenti S, et al. Consensus on the use of the fixed combination calcipotriol/betamethasone dipropionate in the treatment of plaque psoriasis. *G Ital Dermatol Venereol*. 2012;147:609-24.
15. Rigopoulos D, Gregoriou S, Stratigos A, Larios G, Korfitis C, Papaioannou D, et al. Evaluation of the efficacy and safety of infliximab on psoriatic nails: an unblinded, nonrandomized, open-label study. *Br J Dermatol*. 2008;159:453-6.
16. Rigopoulos D, Gregoriou S, Makris M, Ioannides D. Efficacy of ustekinumab in nail psoriasis and improvement in nail-associated quality of life in a population treated with ustekinumab for cutaneous psoriasis: an open prospective unblinded study. *Dermatology*. 2011;223:325-9.
17. Stefanaki C, Lagogianni E, Kontochristopoulos G, Verra P, Barkas G, Katsambas A, et al. Psoriasis in children: a retrospective analysis. *J Eur Acad Dermatol Venereol*. 2011;25:417-21.
18. Rigopoulos D, Gregoriou S, Katrinaki A, Korfitis C, Larios G, Stamou C, et al. Characteristics of psoriasis in Greece: an epidemiological study of a population in a sunny Mediterranean climate. *Eur J Dermatol*. 2010;20:189-95.
19. Devaux S, Castela A, Archier E, Gallini A, Joly P, Misery L, et al. Adherence to topical treatment in psoriasis: a systematic literature review. *J Eur Acad Dermatol Venereol*. 2012;26:61-7.
20. Ersner SJ, Cowdell FC, Latter SM, Healy E. Self-management experiences in adults with mild-moderate psoriasis: an exploratory study and implications for improved support. *Br J Dermatol*. 2010;163:1044-9.
21. Swinburn P, Lloyd A, Boye KS, Edson-Heredia E, Bowman L, Janssen B. Development of a disease-specific version of the EQ-5D-5L for use in patients suffering from psoriasis: lessons learned from a feasibility study in the UK. *Value Health*. 2013;16:1156-62.
22. Pattanaphesaj J, Thavorncharoensap M. Measurement properties of the EQ-5D-5L compared to EQ-5D-3L in the Thai diabetes patients. *Health Qual Life Outcomes*. 2015;13:14.
23. Mease PJ, Menter MA. Quality-of-life issues in psoriasis and psoriatic arthritis: outcome measures and therapies from a dermatological perspective. *J Am Acad Dermatol*. 2006;54:685-704.
24. Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI)-a simple practical measure for routine clinical use. *Clin Exp Dermatol*. 1994;19:210-6.
25. Langley RG, Ellis CN. Evaluating psoriasis with Psoriasis Area and Severity Index, Psoriasis Global Assessment, and Lattice System Physician's Global Assessment. *J Am Acad Dermatol*. 2004;51:563-9.
26. Van de Kerkhof PC. The impact of a two-compound product containing calcipotriol and betamethasone dipropionate (Daivobet/ Dovobet) on the quality of life in patients with psoriasis vulgaris: a randomized controlled trial. *Br J Dermatol*. 2004;151:663-8.
27. Ortonne JP, Ganslandt C, Tan J, Nordin P, Kragballe K, Segaeert S. Quality of life in patients with scalp psoriasis treated with calcipotriol/betamethasone dipropionate scalp formulation: a randomized controlled trial. *J Eur Acad Dermatol Venereol*. 2009;23:919-26.
28. Sticherling M, Eicke C, Anger T. Practicability of combined treatment with calcipotriol/betamethasone gel (Daivobet(R) Gel) and improvement of quality of life in patients with psoriasis. *J Dtsch Dermatol Ges*. 2013;11:420-7.
29. Shikhar R, Willian MK, Okun MM, Thompson CS, Revicki DA. The validity and responsiveness of three quality of life measures in the assessment of psoriasis patients: results of a phase II study. *Health Qual Life Outcomes*. 2006;4:71.
30. Buckley C, Hoffmann V, Shapiro J, Saari S, Cambazard F, Milsgaard M. Calcipotriol plus betamethasone dipropionate scalp formulation is effective and well tolerated in the treatment of scalp psoriasis: a phase II study. *Dermatology*. 2008;217:107-13.
31. van de Kerkhof PC, Hoffmann V, Anstey A, Barnes L, Bolduc C, Reich K, et al. A new scalp formulation of calcipotriol plus betamethasone dipropionate compared with each of its active ingredients in the same vehicle for the treatment of scalp psoriasis: a randomized, double-blind, controlled trial. *Br J Dermatol*. 2009;160:170-6.
32. McCormack PL. Calcipotriol/betamethasone dipropionate: A review of its use in the treatment of psoriasis vulgaris of the trunk, limbs and scalp. *Drugs*. 2011;71:709-30.
33. Douglas WS, Poulin Y, Decroix J, Ortonne JP, Mrowietz U, Gulliver W, et al. A new calcipotriol/betamethasone formulation with rapid onset of action was superior to monotherapy with betamethasone dipropionate or calcipotriol in psoriasis vulgaris. *Acta Derm Venereol*. 2002;82:131-5.
34. Claréus BW, Houwing R, Sindrup JH, Wigchert S. The DESIRE study - Psoriasis patients' satisfaction with topical treatment using a fixed combination of calcipotriol and betamethasone dipropionate in daily clinical practice. *Eur J Dermatol*. 2009;19:581-5.
35. Carroll CL, Feldman SR, Camacho, R. Balkrishnan. Better medication adherence results in greater improvement in severity of psoriasis. *Br J Dermatol*. 2004 Oct;151:895-7.
36. Ulf E, Maroti M, Kettis-Lindblad A, Kjellgren KI, Ahlner J, Ring L, et al. Single application of a fluorescent test cream by healthy volunteers: assessment of treated and neglected body sites. *Br J Dermatol*. 2007;156:974-8.
37. Serup J, Lindblad AK, Maroti M, Kjellgren KI, Niklasson E, Ring L, et al. To follow or not to follow dermatological treatment--a review of the literature. *Acta Derm Venereol*. 2006;86(3):193-7.
38. Saraceno R, Camplone G, D'Agostino M, De Simone C, Di Cesare A, Filosa G, et al. Efficacy and maintenance strategies of two-compound formulation calcipotriol and betamethasone dipropionate gel (Xamiol(R) gel) in the treatment of scalp psoriasis: results from a study in 885 patients. *J Dermatolog Treat*. 2014;25:30-3.
39. Colombo GL, Di Matteo S, Bruno G, Girolomoni G, Vena GA. Calcipotriol and betamethasone dipropionate in the treatment of mild-to-moderate psoriasis: a cost-effectiveness analysis of the ointment versus gel formulation. *Clinicoecon Outcomes Res*. 2012;4:261-8.

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