Medication Formulation Affects Quality of Life: A Randomized Single-Blind Study of Clobetasol Propionate Foam 0.05% Compared With a Combined Program of Clobetasol Cream 0.05% and Solution 0.05% for the Treatment of Psoriasis

Kendra Gail Bergstrom, MD; Karina Arambula, BA; Alexa Boer Kimball, MD, MPH

For topical medications commonly used to treat dermatologic conditions, outcomes may be affected by the choice of delivery vehicles. The aim of this study was to compare quality of life (QOL), effectiveness, user satisfaction, and cost-effectiveness of 2 clobetasol regimens for the treatment of psoriasis over 14 days. In a single-blind design, 32 patients randomized into 2 groups applied either clobetasol foam 0.05% to the skin and scalp or combination clobetasol cream 0.05% to the skin and clobetasol solution 0.05% to the scalp. Psoriasis severity was measured using the standardized Psoriasis Area and Severity Index (PASI) and self-administered PASI (SAPASI). QOL was assessed via the EuroQoL-5D (EQ-5D) questionnaire and Dermatology Life Quality Index (DLQI). Cost-effectiveness was measured by the amount of medication used per body surface area (BSA) treated and by cost per point improvement in PASI score.

In this study, a foam formulation performed better than a cream/solution combination by several measures. A greater absolute improvement in psoriasis severity was seen in the group using the foam than in the group using the cream/solution (mean decrease in PASI=5.0 vs 3.3, P=*.05). The PASI score in the foam group decreased by 41% versus 35% in the cream/solution group (*P=*.17). In scalp psoriasis, the group using the foam had greater improvement in both absolute (*P=*.03) and percentage (*P=*.03) terms and than the solution group. When measuring global QOL, foam users had a significantly greater increase in EQ-5D than those using the cream/solution in absolute (*P=*.05,* P=*.02) and percentage (*P=*.04,* P=*.02) terms (first and second survey components, respectively). Differences in improvement of skin-specific QOL, quantified by DLQI scores between groups, were suggested but not statistically significant. Patients using foam spent less time applying medication compared with previous topical medications (*P<*.001). No significant difference in cost was appreciated between foam and cream/solution over the period after controlling for BSA ($8.18 vs $7.05 per percentage BSA affected,* P=*.30).*

Cutis. 2003;72:407-411.

Accepted for publication March 27, 2003.

From the Department of Dermatology, Stanford University, California.

This research was supported by an unrestricted grant from the Connetics Corporation. Drs. Bergstrom and Arambula report no conflict of interest. Dr. Kimball is a paid consultant for Connetics Corporation.

Reprints: Alexa Boer Kimball, MD, MPH, Department of Dermatology, Stanford University, 900 Blake Wilbur Dr, Stanford, CA 94305-5334 (e-mail: akimball@stanford.edu).

Psoriasis is usually a lifelong condition, requiring years if not decades of treatment. Despite therapy, most patients with psoriasis never experience clinical remission,[1] and those with even moderate disease report a significantly decreased quality of life (QOL) when compared with healthy adult volunteers. Significantly decreased scores have been reported on QOL indices, such as the EuroQoL-5D (EQ-5D), Short Form-36, and Dermatology Life Quality Index (DLQI).[2] Severe psoriasis also can be associated with depressive symptoms; in one study, 10% of patients ranging in age from 18 to 34 years reported contemplating suicide at some point.[2]

Recently, a foam form of clobetasol propionate 0.05% (Olux®) was found to be as effective as clobetasol propionate solution 0.05% for the treatment of moderate to severe scalp psoriasis.[3] This study was designed to test whether or not different formulations of the same medication—topical clobetasol propionate—would affect measurable outcomes.

Patients and Methods

In a single-blind design, 32 patients were randomized into 2 treatment groups. One group applied clobetasol foam to affected skin and scalp, and another group applied clobetasol cream to the skin and clobetasol solution to the scalp for a 14-day period. Stanford University's Panel on Human Subjects approved the study for a period of 6 months between January and June 2001. Patients were assessed at the baseline visit and the second (final) visit for psoriasis area, disease severity, and QOL indices (EQ-5D and DLQI). Patients returned their unused medication and completed a questionnaire assessing their compliance, satisfaction, and ease of medication use.

Study patients were older than 18 years, with stable or worsening psoriasis covering at least 3% of body surface area (BSA), including both the skin and scalp. The face, genitalia, and intertriginous areas were excluded from treatment. To minimize interactions with prior treatments, a 2-week washout period of topical agents and a 4-week washout period of oral medications were required. Seven women and 25 men (mean age: 49 years) were enrolled in the study. Of the 32 patients, 3 were excluded because of noncompliance as follows: 1 did not return for a second visit, 1 misapplied the foam, and 1 applied the medication intermittently over a 3-week period.

All patients were residents of the San Francisco Bay area. There were no statistically significant differences between the groups. Patient demographics are shown in Table 1. Socioeconomic status did not affect patient participation, as patients were distributed across different income groups and educational backgrounds.

Table 1.

Demographics of Evaluable Patients

	n=29
Gender, n (%)	
Male	23 (79)
Female	6 (21)
Race/ethnicity, n (%)	
White	20 (69)
Black	2 (7)
Hispanic	6 (21)
Pacific Islander	1 (3)
Marital status, n (%)	
Single	10 (34)
Married	17 (59)
Divorced or widowed	2 (7)
Education, n (%)	
<High school	2 (7)
High school degree	5 (17)
Vocational school degree	9 (31)
College degree	10 (34)
Professional degree	3 (10)
Employment, n (%)*	
Employed	21 (72)
Unemployed	2 (7)
Retired	4 (14)
Annual income bracket, n (%)†	
Lowest (<$25,000/y)	7 (24)
Lower middle ($25,000–$50,000/y)	7 (24)
Upper middle ($50,000–$100,000/y)	6 (21)
Highest (>$100,000/y)	6 (21)

*Two patients (7%) declined to specify.
†Three patients (10%) declined to specify.

Severity of disease was evaluated using the Psoriasis Area and Severity Index (PASI), a scoring index that weighs the severity of 3 intensity measures (erythema, induration, and scale) with percentage BSA affected. The range of scores

possible is 0 to 72; mild psoriasis is sometimes defined as PASI less than 10, and moderate psoriasis as at least 10.[4] Mean PASI score at baseline was 12.3 (SD=8.0) in the foam group and 9.6 (SD=4.8) in the cream/solution group.

The self-administered PASI (SAPASI) was used to evaluate patients' perception of their skin changes. The SAPASI parallels the PASI by asking patients to perform the same assessment of their skin. Over time and changes in disease, the SAPASI parallels and tracks the PASI.[5,6] The mean baseline SAPASI was 15.3 (SD=7.6) in the foam group and 16.2 (SD=15.9) in the cream/solution group.

QOL was evaluated using both a global health assessment, the EQ-5D validated survey instrument, and the DLQI, a skin-specific survey. The EQ-5D was developed to compare QOL and global functioning over different disease states.[7,8] The EQ-5D consists of a questionnaire and a visual analog scale of 0 (worst imaginable health state) to 100 (best imaginable health state). The DLQI is a skin-specific survey developed in 1994 based on the responses of patients to questions about the impact their skin disease and its treatment has had on their lives, which allow comparisons between different time points and skin diseases.[9] Scoring ranges from 0 to 30 and is specific to skin diseases, with healthy volunteers scoring an average of 0.5 on the scale.[9]

Cost of treatment was evaluated by first calculating the amount of medication used (in grams) over the 2-week period. Then, the cost of treatment (amount used × cost/gram) was divided by the total percentage BSA treated to find the cost of treating 1% BSA.

All data were analyzed at the completion of the study using Excel software. Two-tailed tests were performed; $P<.05$ was considered statistically significant.

Results

Clobetasol foam was more effective than cream/solution for absolute improvement in disease (mean decrease in PASI score=5.0 vs 3.3, respectively; $P=.05$). The PASI score in the foam group decreased by 41% versus 35% in the cream/solution group ($P=.17$)(Table 2). For the treatment of body psoriasis, the 2 treatments were equally effective in treating erythema ($P=.33$), induration ($P=.12$), and scale ($P=.41$). Change in patient-reported disease, as measured by the SAPASI, was similar in both groups. Scores decreased by 4.5 (22%) in the foam group and by 4.3 (20%) in the cream/solution group ($P=.49$ in absolute improvement and $P=.46$ in percentage improvement). Reported compliance was similar between the 2 groups. For the treatment of scalp psoriasis, the foam was more effective than the solution in both absolute ($P=.03$) and percentage ($P=.03$) improvements.

When comparing QOL, patients using clobetasol foam showed more improvement in EQ-5D scores than in those using cream/solution in both absolute ($P=.05$ and $P=.02$) and percentage terms (first and second survey components, respectively). All patients showed improved QOL, as measured by the DLQI, over the 2-week period. A difference in the improvement of DLQI scores between the 2 groups was suggested but not significant, with improvement of 5 points (45%) with foam and 3 points (29%) with cream/solution, (absolute, $P=.10$; percentage, $P=.13$).

For all treated patients using any formulation of clobetasol, disability decreased by an average of 4.0 (on a scale of 30) on the DLQI and 0.41 (out of 15) in the first component of the EQ-5D and 6 (out of 100) in the second component. These improvements corresponded to a decrease of 4.1 in PASI score over the same period.

At the second visit, study participants were asked about their medication preferences and opinion of absolute and relative effectiveness. In addition, questions were asked about time of application, number of treatments missed, and specific improvement in appearance, pain, and itching. Patients using foam reported significantly less time spent applying the medication compared with other topical medications ($P=.001$). In contrast, patients using the cream/solution reported spending a similar amount of time applying the medication compared with other topical medications. Patients using the foam had a significantly better relative impression of the medication compared with other topical medications ($P=.03$). Pain of treated skin showed more improvement with the foam than with the cream/solution ($P=.02$). Patients reported that the foam was relatively more effective than the cream/solution compared with other medications ($P=.04$). The 2 groups were similar in improvement of self-described skin appearance, itching symptoms, relative and absolute satisfaction with treatment, and overall impression of medication.

After controlling for BSA, there was no statistically significant difference in cost between foam and cream/solution over the 2-week period ($8.18 vs $7.05 per 1% BSA affected, respectively; $P=.30$) (Table 2). The cost per change of one unit in PASI score was $21.60 for patients using foam and $16.42 for those using cream/solution; the difference was not statistically significant ($P=.20$).

Table 2.

Comparison of Clobetasol Foam Group Versus Combination Cream/Solution Group*

Variable	Foam Users	Cream/Solution Users	*P* Value
Skin changes, mean (%)			
PASI	−4.97 (−41)	−3.32 (−35)	.048
Scalp PASI	−1.03 (−76)	−0.45 (−47)	.026
Body PASI	−4.86 (−44)	−7.33 (−82)	.010
% BSA	−3.4% (−27)	−2.8% (−21)	.143
QOL			
DLQI	−5.14 (−45)	−3.06 (−29)	.098
EQ-5D, component 1	−0.71 (−33)	−0.13 (−8)	.049
EQ-5D, component 2†	9.35 (28)	2.66 (4)	.019
Cost			
Cost to treat 1% BSA	$8.18	$7.05	.300
Grams of medication per % BSA treated	7.43 g	10.16 g	.130
Cost per 1-point change in PASI score	$21.60	$16.42	.197

*PASI indicates Psoriasis Area and Severity Index; BSA, body surface area; QOL, quality of life; DLQI, Dermatology Life Quality Index; EQ-5D, EuroQoL-5D.

†The EQ-5D, component 2, is a positive measure of QOL, in contrast to the DLQI and EQ-5D, component 1, which quantify disability.

Comment

The study of the cost of medical care, patient satisfaction, and effect of therapy on QOL is a relatively young field compared with the study of therapeutic efficacy. Nonetheless, these outcome measures have become increasingly important, as healthcare systems struggle with providing adequate care at a reasonable cost.[10] New medications or formulations often are touted to be more effective than older versions but usually come at a higher cost. The question, then, is whether they are worth the cost and how to evaluate therapeutic value.

Specifically, the clobetasol foam was generally more effective than the clobetasol cream/solution combination for the treatment of mild to moderate psoriasis. The increased improvement in clinical severity, decreased application time, and increased perception of relative efficacy, combined with similar cost of treatment, suggests that clobetasol foam is a better choice than cream/solution for this group of patients. Adverse effects were minimal for all formulations and consisted primarily of a burning sensation for a few seconds after foam application, which resolved in the first week of treatment.

A difference between groups was suggested but not significant as reported in the DLQI, which asks about more specific issues, such as dressing, swimming, and difficulty applying medications. The small sample size may have masked a true difference between these populations. Differences in outcomes between genders were not significant and were consistent with past findings.[11,12] As seen in previous studies, individual QOL did not always correlate well with changes in PASI scores, but on an aggregate level, there were statistically significant changes in both outcome measures.[13] The discrepancy between "disease improvement" and "less improvement" in QOL may be explained by the fact that transient (14 day) symptom improvement, a limitation of this study, does not necessarily change the outlook, prognosis, or restrictions on daily activities imposed by a lifelong condition.

For chronic conditions such as psoriasis, QOL status can be used to evaluate therapeutic efficacy. Because the impact on daily life is a significant predictor of noncompliance with topical medication regimens,[14] increasing QOL may better predict outcomes in response to a given therapy. Further characterization of the interaction among clinical effectiveness, QOL, and cost will help researchers and clinicians evaluate therapeutic choices for psoriasis and other skin diseases.

Acknowledgment—The authors would like to thank Duc-Uy Dang for providing support to the project.

REFERENCES

1. Ramsay B, O'Reagan M. A survey of the social and psychological effects of psoriasis. *Br J Dermatol*. 1988;118:195-201.
2. Krueger G, Koo J, Lebwohl M, et al. The impact of psoriasis on quality of life: results of a 1998 National Psoriasis Foundation patient-membership survey. *Arch Dermatol*. 2001;137:280-284.
3. Melian EB, Spencer CM, Jarvis B. Clobetasol propionate foam, 0.05%. *Am J Clin Dermatol*. 2001;2:89-92.
4. Fredricksson TPU. Severe psoriasis: oral therapy with a new retinoid. *Dermatologica*. 1978;157:238-244.
5. Feldman SR. Fleischer AB Jr., Reboussin DM, et al. The self-administered psoriasis area and severity index is valid and reliable. *J Invest Dermatol*. 1996;106:183-186.
6. Fleischer AB Jr, Feldman SR, Dekle CL. The SAPASI is valid and responsive to psoriasis disease severity changes in a multi-center clinical trial. *J Dermatol*. 1999;26:210-215.
7. Group TE. EuroQoL—a new facility for the measurement of health-related quality of life: the EuroQuol Group. *Health Policy*. 1990;16:199-208.
8. Rabin R, de Charro F. EQ-5D: a measure of health status from the EuroQoL Group. *Ann Med*. 2001;33:337-343.
9. Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI)—a simple practical measure for routine clinical use. *Clin Exp Dermatol*. 1994;19:210-216.
10. Krueger GG, Feldman SR, Camisa C, et al. Two considerations for patients with psoriasis and their clinicians: what defines mild, moderate, and severe psoriasis? what constitutes a clinically significant improvement when treating psoriasis? *J Am Acad Dermatol*. 2000;43:281-285.
11. Gupta MA, Gupta AK. Age and gender differences in the impact of psoriasis on quality of life. *Int J Dermatol*. 1995;34:700-703.
12. Lundberg L, Johannesson M, Silverdahl M, et al. Health-related quality of life in patients with psoriasis and atopic dermatitis measured with SF-36, DLQI and a subjective measure of disease activity. *Acta Derm Venereol*. 2000;80:430-434.
13. Touw CR, Hakkaart-Van Roijen L, Verboom P, et al. Quality of life and clinical outcome in psoriasis patients using intermittent cyclosporin. *Br J Dermatol*. 2001;144:967-972.
14. Richards HL, Fortune DG, O'Sullivan TM, et al. Patients with psoriasis and their compliance with medication. *J Am Acad Dermatol*. 1999;41:581-583.