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A comparison of treatment with dithranol and calcipotriol on the clinical severity and quality of life in patients with psoriasis

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Summary

In a multicentre, randomized, open study, 306 patients of either sex, over 18 years of age with stable chronic plaque psoriasis > 100 cm^2 in surface area, and who gave informed consent, applied Dovonex (calcipotriol) ointment (50 μg/g) twice daily or Dithrocream (short-contact dithranol) 0·1–2% for up to 3 months. The number of patients 'cleared' or with 'marked improvement' at the end of treatment were: investigators' assessment—calcipotriol 92 of 153 (60·1%); dithranol 67 of 131 (51·1%); odds ratio 1·44 [95% confidence interval (CI) 0·90, 2·31; $P = 0·128$]; patients' assessment—calcipotriol 93 of 153 (60·8%); dithranol 65 of 131 (49·6%); odds ratio 1·57 (95% CI 0·98, 2·52; $P = 0·059$). Significant improvement in patients' quality of life as assessed by the Psoriasis Disability Index (PDI) and the Sickness Impact Profile (SIP) were seen in both treatment groups. Reduction in the total mean score for PDI was 6·5 in the calcipotriol group (95% CI 4·4, 8·6; $P = 0·001$) and 3·7 in the dithranol group (95% CI 1·1, 6·3; $P = 0·005$). The reduction in the total mean score for SIP was 2·8 in the calcipotriol group (95% CI 1·4, 4·3; $P < 0·001$) and 1·7 in the dithranol group (95% CI 0·2, 3·1; $P = 0·024$). Calcipotriol treatment tended to have advantages over treatment with dithranol in improving quality of life.

Psoriasis affects about 2% of the population in Britain.[1,2] As well as the clinical effects of the condition (scaling, redness, irritation), psoriasis has a considerable effect on the quality of life of those affected. Psychosocial effects such as embarrassment, self-consciousness and feeling of shame and rejection by others may impinge markedly on leisure and even work in some cases.[3,4] The degree of emotional upset and psoriasis-specific stress are largely independent of disease severity.[5,6]

The effect of psoriasis on patients' quality of life has been assessed by Finlay *et al.*[7] using a specially designed and validated questionnaire, termed the Psoriasis Disability Index (PDI). Recently, Koo[8] has developed another disease-specific questionnaire, termed the Psoriasis Quality of Life Questionnaire. Other, more general, quality of life measures, such as the Sickness Impact Profile (SIP)[9] and the SF-36 questionnaire,[10] have also been used. There are few data on the effect of anti-psoriatic treatment on patients' quality of life, apart from the preliminary study on the PDI by Finlay and Kelly.[11]

The present study aimed to assess the quality of life of patients with psoriasis before and after treatment with calcipotriol ointment or a 'short-contact' dithranol regimen. The comparative clinical efficacy of the two treatments and the relative changes in the quality of life measures associated with treatment are presented in this report. A more detailed analysis of the results of quality of life measures before treatment will be presented elsewhere.

Subjects and methods

This was a prospective, multicentre, randomized, open study and included patients of either sex, over 18 years of age with a clinical diagnosis of stable, mild to moderate chronic plaque psoriasis of at least 100 cm^2 surface area, but less than 40% of body surface, who had attended their general practitioner's surgery in the past 6 months for psoriasis. Excluded were patients with acute guttate or pustular psoriasis, chronic plaque psoriasis affecting the face and scalp only, anyone prescribed topical antipsoriatic treatment in the 2-week period before visit 1 or systemic treatment in the previous 8 weeks, patients who were pregnant or breastfeeding, patients receiving > 400 iu of vitamin D

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daily or prescribed calcium tablets or any other medication that would have affected the course of the disease. Also excluded were patients known to be hypersensitive to trial medication and those likely to be non-compliant with the study protocol or currently participating in another clinical trial. The study was approved by local ethics committees.

Treatment

Patients received at random 3 months' treatment with either Dovonex ointment containing 0·005% calcipotriol applied twice daily or Dithrocream containing 0·1%, 0·25%, 0·5%, 1·0% and 2·0% dithranol applied once daily for 30 min to 1 h. The concentration of dithranol was increased step by step at weekly intervals until either: (i) complete clearance of the patients' psoriatic lesions was attained, or (ii) unacceptable local side-effects appeared, in which case the concentration used was reduced by one step.

Assessments

The overall clinical response was assessed by both the investigator and the patient as 'cleared', 'marked improvement', 'some improvement', 'no change' or 'worse' at the end of treatment. Quality of life assessments were conducted before treatment commenced and at the end of treatment using the Psoriasis Disability Index (PDI) and the Sickness Impact Profile (SIP). The PDI[7] questionnaire comprises 15 questions under the following headings: daily activities (five questions), work or school (if applicable) or alternative questions (if neither applicable) (three questions), personal relationships (two questions), leisure (four questions) and treatment (one question). Each question is scored on a seven-point scale from 1 (not at all) to 7 (very much). The questions record a patient's symptoms and feelings about their psoriasis during the previous 4 weeks.

The SIP[9] performance-based questionnaire comprises 136 health-related statements divided into 12 sections under the following headings: sleep and rest (seven statements), emotional behaviour (nine statements), body care and movement (23 statements), daily work around the house (10 statements), home management (10 statements), social interaction (20 statements), ambulation (12 statements), alertness behaviour (10 statements), communication (nine statements), work other than housework (nine statements), recreation and pastimes (eight statements) and eating and drinking habits (nine statements). Patients' present health status is also recorded. Patients completed the questionnaire by ticking only those statements that described their health on that day. In general, the more statements that are ticked, the greater the impact of the disease on a patient's quality of life. Patients also assessed their present health status as 'very good', 'good', 'fair', 'poor' or 'very poor'.

Five additional quality of life questions were used to address aspects of psoriasis either not addressed or not addressed in detail in the PDI questionnaire or the SIP questionnaire. The questions related to the impact of the disease on the avoidance of social/leisure facilities (15 questions), the avoidance of facilities such as communal showers and changing rooms (four questions), restriction on clothing (three questions), exclusion from types of work (15 questions) and personal issues (six questions). The questions did not relate to any particular duration of time.

Statistical methods

For comparison of efficacy, the two treatment groups were compared with respect to the proportion of patients for whom the investigators' and the patients' assessment at the end of treatment was 'cleared/marked improvement' using the χ^2-test. The odds ratio with 95% confidence intervals (CIs) was used to estimate the difference between the two treatments. An odds ratio greater than 1·0 indicates an effect in favour of calcipotriol, whereas an odds ratio less than 1·0 indicates an effect in favour of dithranol. For the PDI, each of the five section totals and the overall total were calculated for each patient by summing the question scores. For the SIP and additional quality of life questions, each of the section totals and the overall total were calculated by summing the number of statements ticked.

For each questionnaire, the two treatment groups were compared with respect to the end of treatment minus the before treatment difference for each section total and the overall total using the two-sample *t*-test. The difference between treatments (calcipotriol minus dithranol) was calculated with 95% confidence limits. For each treatment group, a within-treatment comparison of the end of treatment overall total against the before treatment overall total was made using a paired *t*-test, and 95% CIs were calculated for the end of treatment minus the before treatment difference.

Results

A total of 306 patients were recruited, 161 into the

calcipotriol group and 145 into the dithranol group. The two treatment groups were comparable in respect of sex distribution, age, duration of psoriasis and severity of psoriasis (Table 1). There was a trend for the calcipotriol-treated group to contain more patients previously treated with calcipotriol and dithranol when compared with the dithranol-treated group. Eleven patients defaulted and provided no data, and nine patients were allocated the incorrect treatment. Therefore, efficacy data were available on 286 patients (153 calcipotriol, 133 dithranol). Of these, 249 patients (134 calcipotriol, 115 dithranol) completed the quality of life questionnaires before and after treatment. The mean duration of treatment was 12 weeks in the calcipotriol group and 10·8 weeks in the dithranol group. The two treatment groups were comparable in respect of the responses to the quality of life measures before treatment (Table 2).

Clinical efficacy

At the end of treatment, the proportions of patients 'cleared' or with 'marked improvement' were calcipotriol 60·1% (92 of 153) and dithranol 51·1% (67 of 131), two patients not being assessed, odds ratio 1·44 (95% CI 0·90, 2·31; $P = 0·128$). At the end of treatment, the proportions of patients 'cleared' or with 'marked improvement' were calcipotriol 60·8% (93 of 153) and dithranol 49·6% (65 of 131), two patients not being assessed, odds ratio 1·57 (95% CI 0·98, 2·52; $P = 0·059$).

Psoriasis Disability Index

Patients' quality of life as assessed by the PDI improved significantly after both treatments. The reduction in the total mean score for PDI was 6·5 in the calcipotriol group (95% CI 4·4, 8·6; $P = 0·001$) and 3·7 in the

Table 1. Demographics of patients

	Calcipotriol	Dithranol
No. of patients	161	145
Sex		
Male	75	69
Female	86	76
Age (years)		
Mean	47·0	46·3
SD	15·8	15·0
Duration of psoriasis (years)		
Mean	18·0	19·4
SD	12·0	13·0
Previous treatment with calcipotriol (%)	73 (45·3)	57 (39·3)
Previous treatment with dithranol (%)	69 (42·9)	49 (33·8)
Severity of psoriasis [no. of patients (%) with]		
Redness		
Absent	3 (1·9)	2 (1·4)
Mild/moderate	142 (88·2)	125 (86·2)
Severe	16 (9·9)	18 (12·4)
Thickness		
Absent	1 (0·6)	1 (0·7)
Mild/moderate	137 (85·1)	131 (85·6)
Severe	23 (14·3)	12 (8·3)
Scaliness[a]		
Mild/moderate	133 (82·6)	118 (81·9)
Severe	28 (17·4)	26 (18·1)
Extent		
0–10%	60 (37·3)	60 (41·4)
11–20%	61 (37·9)	57 (39·3)
21–30%	28 (17·4)	19 (13·1)
31–40%	12 (7·5)	9 (6·2)

[a] Not assessed in one dithranol-treated patient.

Table 2. Quality of life measures before treatment

	Calcipotriol ($n=134$)	Dithranol ($n=115$)
Psoriasis Disability Index[a] (mean)		
Daily activities	14·7	13·7
Work/school and alternative	4·7	4·7
Personal relationships	3·5	3·5
Leisure	9·4	8·3
Treatment	2·9	2·8
Total score	35·0	33·2
(SD)	(17·1)	(15·9)
Sickness Impact Profile[b]		
Present health status (%)		
Very good	13·4	17·4
Good	46·5	40·4
Fair	33·1	34·9
Poor	4·7	6·4
Very poor	2·4	0·9
Mean total score	10·2	8·9
(SD)	(12·9)	(9·6)
Additional measures[c] (mean)		
Social/leisure activities avoided	2·6	2·1
Facilities avoided	1·3	1·1
Clothing restricted	1·0	1·0
Exclusion from work	0·2	0·1
Personal issues	0·5	0·4

[a] Maximum score 105.
[b] Maximum score 136.
[c] Maximum scores 14, 4, 3, 15 and 6, respectively.

dithranol group (95% CI 1·1, 6·3; $P=0·005$). Mean differences between treatments in the change in score for the individual sections of the PDI and for the total score are shown in Table 3. To assess the validity of the PDI, the mean changes in the PDI in relation to the investigators' assessment of the overall clinical response were determined. In patients 'cleared', the mean change in the PDI was $-10·9$, in those with 'marked improvement' $-8·0$, in those with 'some improvement' $-2·3$ and, in patients assessed as 'no change' or 'worse', the mean changes were $+2·4$ and $+3·0$, respectively.

Sickness Impact Profile

Patients' perception of their current health status did not appear to change on either treatment. In the calcipotriol-treated group, the proportions of patients who considered their health 'fair' or better was 92·9% before treatment and 92·1% after treatment. In the dithranol-treated group, the proportions were 92·7% before treatment and 96·3% after treatment. Patients' quality of life as assessed by the SIP improved significantly after both treatments. The reduction in the total score for the SIP was 2·8 in the calcipotriol group (95% CI 1·4, 4·3; $P<0·001$) and 1·7 in the dithranol group (95% CI 0·2, 3·1; $P=0·024$). Mean differences between treatments in the change in score for the individual sections of the SIP and for the total score are shown in Table 4. To assess the validity of the SIP, the mean changes in the SIP in relation to the investigators' assessment of the overall clinical response were determined. In patients 'cleared', the mean change in the SIP was $-2·3$, in those with 'marked improvement' $-2·1$, in those with 'some improvement' $-3·1$ and, in patients assessed as 'no change' or 'worse', the mean changes were $-0·2$ and $-2·9$, respectively.

Additional quality of life questionnaire

Over two-thirds of patients avoided certain social/leisure activities, mainly swimming and sunbathing, because of their disease. Similar proportions of sufferers avoided using communal changing rooms and short-sleeved or

Table 3. Psoriasis Disability Index:[a] difference (calcipotriol–dithranol) in change in mean scores from before treatment to end of treatment

	Mean difference	95% CI	P[b]
Daily activities	−2·0	−3·5, −0·5	0·010
Work/school and alternative	−0·1	−0·9, 0·7	0·793
Personal relationships	−0·3	−0·9, 0·3	0·362
Leisure	−0·5	−1·6, 0·7	0·417
Treatment	−0·4	−0·9, 0·1	0·083
Total score	−2·8	−6·1, 0·5	0·091

[a] Scored: Daily activities 5–35, work/school and alternative 3–21; personal relationships 2–14; leisure 4–28; treatment 1–7.
[b] From two-sample *t*-test.

Table 4. Sickness Impact Profile:[a] difference (calcipotriol–dithranol) in change in mean scores from before treatment to end of treatment

Section of SIP	Mean difference	95% CI	P^b
Sleep and rest	−0·1	−0·34, 0·14	0·430
Emotional behaviour	0·07	−0·25, 0·39	0·663
Body care and movement	−0·33	−0·72, 0·06	0·101
Daily work around the house	0·02	−0·29, 0·32	0·915
Home management	−0·20	−0·40, 0·00	0·056
Social interaction	−0·37	−1·01, 0·27	0·259
Ambulation	0·06	−0·17, 0·28	0·621
Alertness behaviour	−0·12	−0·50, 0·26	0·537
Communication	−0·01	−0·19, 0·17	0·918
Work other than housework	0·03	−0·16, 0·21	0·753
Recreation and pastimes	−0·07	−0·42, 0·28	0·691
Eating and drinking habits	−0·12	−0·26, 0·01	0·078
Total score	−1·1	−3·2, 0·9	0·273

[a] Maximum of 136.
[b] From two-sample *t*-test

summer wear. Personal issues such as making new friends, personal relationships and sexual difficulties arose in 10–15% of patients. Patients' quality of life related to the use of social/leisure activities improved significantly after both treatments. The reduction in the score for social/leisure activities avoided was 0·63 (2·60, 1·97) in the calcipotriol group (95% CI 0·31, 0·96; $P<0·001$) and 0·50 (2·05, 1·55) in the dithranol group (95% CI 0·20, 0·79; $P=0·001$).

Patients' quality of life related to use of facilities and personal issues improved significantly after treatment with calcipotriol, but not after treatment with dithranol. In calcipotriol-treated patients, the reduction in the score for facilities avoided was 0·22 (1·32, 1·10) in the calcipotriol group (95% CI: 0·07, 0·38; $P=0·004$). The reduction in the score for personal issues was 0·10 (0·45, 0·35) in the calcipotriol group (95% CI 0·01, 0·19; $P=0·03$). Neither treatment had any statistically significant effect on the scores for restrictions on clothing or exclusion from types of work. None of the mean differences between treatments in the change in score for the individual questions approached statistical significance.

Discussion

This study evaluated the efficacy and effect on patients' quality of life of two well-documented topical treatments for plaque psoriasis, calcipotriol ointment and short-contact dithranol cream. Both treatments had a statistically significant beneficial effect on the quality of life measures in patients with plaque psoriasis. Calcipotriol was superior to dithranol in some respects. The assessment of efficacy by both the investigator and the patient was strongly in favour of calcipotriol (calcipotriol: investigator 60·1%, patient 60·8%; dithranol: investigator 51·1%, patient 49·6%). In a previously published study, calcipotriol ointment was found to be more effective clinically than short-contact dithranol cream in patients with plaque psoriasis.[12] The response to calcipotriol ointment seen in the present study was similar to that reported previously,[12,13] whereas the response to short-contact dithranol appeared to be somewhat greater than in a previous study.[12] Quality of life was assessed using two well-accepted and previously validated questionnaires, the PDI[7] and the U.K. version of the SIP (U.K. SIP).[9]

Previous studies have shown that psoriasis has an adverse effect on patients' quality of life, and this has been demonstrated particularly using the PDI.[6,7,10,11,14] In this study, use of the PDI has again confirmed the measurable disability that patients suffer because of their psoriasis. The mean PDI score of 34 recorded before treatment is consistent with that determined previously in psoriatic patients.[7]

The impact of psoriasis on patients' quality of life, as measured by the U.K. SIP, was less than that indicated by the PDI. Similar observations have been made previously.[7] One possible explanation could be that, in the U.K. SIP, the questions relate to the day the questionnaire is completed, whereas the PDI covered the preceding 4 weeks. It could be expected that a questionnaire covering a broader time period would be more successful in assessing disability. However, a more likely explanation is that the SIP is a more general measure of health rather than a disease-specific one. It

is also primarily a performance- and activity-based questionnaire. Therefore, it is unlikely to be scored highly by patients with mild to moderate psoriasis, who are generally quite healthy and active.

Assessment of other aspects of quality of life not covered by either the PDI or SIP confirmed the impact that psoriasis has on people's lives. Interference with social and leisure activities was common, and personal relationships were adversely affected in a significant number of patients. Similar observations have been recorded by Koo.[8] The study investigated the change in quality of life measures after treatment with calcipotriol and dithranol. Using the PDI, this study has shown that patients' quality of life improved significantly after treatment with either calcipotriol ($P < 0{\cdot}001$) or dithranol ($P = 0{\cdot}005$). Calcipotriol ointment was superior to dithranol in respect of those aspects of the PDI relating to daily activities ($P = 0{\cdot}010$). It has been suggested that the PDI is less suitable for use in patients with mild to moderate psoriasis,[8] such as those included in this study. Our findings do not support this view. The mean change in the PDI was related to the clinicians' assessment of clinical efficacy, confirming that the PDI is a suitable questionnaire for assessing the quality of life of general practice psoriasis patients.

Using the SIP showed that quality of life improved significantly after treatment with calcipotriol ($P < 0{\cdot}001$) or dithranol ($P = 0{\cdot}02$). However, using this general instrument, the differences between treatments were small and unlikely to be of practical importance. The mean change in the SIP, which is not a disease-specific measure, appeared to be unrelated to the overall clinical response. This finding was not unexpected, as the SIP has been shown previously not to correlate with the severity of psoriasis.[7] A significant improvement in other quality of life aspects, not covered by either the PDI or SIP, was seen in patients given calcipotriol ointment treatment. There were improvements in measures of social and leisure activities ($P < 0{\cdot}001$), use of facilities such as communal showers avoided by having psoriasis ($P = 0{\cdot}004$) and in personal issues ($P = 0{\cdot}032$). After dithranol treatment, there was significant improvement only in respect of social and leisure activities ($P = 0{\cdot}001$). There was no statistically significant difference between treatments in respect of any improvement in these additional activities or issues.

Despite the significant improvement seen in patients' quality of life as assessed by the various questionnaires, it should be noted that there was little effect on patients' perception of their overall health, which was generally perceived as fair to very good. The present study did not include a placebo treatment group, and it could be argued that the improvement in quality of life we observed was caused by a placebo effect. We consider this unlikely for the following reason. Calcipotriol ointment has been shown previously to be significantly more effective clinically than placebo ointment.[13] The degree of clinical improvement seen in this study was related to the magnitude of the improvement in quality of life, as assessed by the PDI. Therefore, it seems reasonable to conclude that the changes in patients' quality of life were probably treatment related. Patients with plaque psoriasis who are treated with either calcipotriol or short-contact dithranol have significantly improved quality of life, with calcipotriol treatment tending to have an advantage over dithranol.

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