Outpatient Treatment with Short-contact Dithranol. The Impact of Frequent Concentration Adjustments

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Short-contact therapy with dithranol has become an important possibility for the treatment of psoriasis on an outpatient basis. Two groups of patients with chronic stable plaque psoriasis were treated on an outpatient basis with a short-contact regime using dithranol in a stiffened paraffin base. In one group the concentrations were adjusted once a week and in the other group 3 times a week. Clinical results were evaluated using the Psoriasis Area Severity Index. In the group of patients which was seen 3 times a week, the improvement was significantly better. The duration of the treatment period was significantly shorter compared to the group seen once a week due to the shorter time interval in which the optimal concentration of dithranol was reached. In addition, the incidence and severity of irritation was more pronounced in the latter group. *Key words: Psoriasis; Anthralin; Treatment protocol.*

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During the last decade short-contact therapy with dithranol has reached the status of a classical treatment of psoriasis (1, 2). The limited application periods permit treatment on an outpatient basis (3, 4). Although the value of short-contact therapy has been established in many studies (5, 6, 7), no consensus has been reached as to guidelines for outpatient management of dithranol treatment. Irritation of the skin prohibits frequent concentration increments. However, if concentration increments are managed too cautiously, the treatment period is unacceptably long and the ultimate effectivity might be limited due to habituation or poor patient compliance.

In the present study, patients were treated with short contact therapy on an outpatient basis. Patients themselves or their partners applied dithranol daily on the skin lesions. Two protocols for outpatient dithranol treatment were compared, in which one group of patients was seen once a week (group 1/w) and the other group three times a week (group 3/w). Concentrations of dithranol were increased only at control visits. Clinical results (clearing and required treatment period) as well as side-effects (irritation and staining) of both groups were monitored in order to assess the effect of frequent concentration adjustments.

METHODS

Patients

Twenty-six patients with chronic stable plaque psoriasis were selected from the outpatient clinic (15 men, 11 women, aged 18–70 years). All patients were untreated for at least one month with respect to topical medications and no systemic anti-psoriatic medication had been taken during the previous year. The percentage of the body surface involved with psoriasis ranged from 5–60%. The patients were allocated at random in two groups. Each group was treated according to one of the following treatment protocols.

Treatment protocols

The first group (16 patients) was treated on a weekly basis (group 1/w). Dithranol was applied daily by the patient himself, left on the plaques for 20 min and subsequently removed using arachis oil and an acidic soap. To avoid drying of the skin, a bland emollient (aqueous cream) was applied after treatment. During the first week, all patients in this group used Psoricreme® (Essex, Amstelveen, The Netherlands) in concentrations of 0.1% (for 3 days) and 0.25% (for 4 days). During the following weeks increasing concentrations of dithranol (0.5%, 1%, 2%, 3%, 4% and 5%) were used in a base described by Seville (8) containing 2% salicylic acid, 30% paraffin solidum and supplied to 100% with vaseline album. At every control visit a decision was made whether the patient could use a higher concentration of dithranol or not. Criteria for remaining at the same concentration were signs of slight irritation, such as increased erythema of the plaque and surrounding skin. Patients were instructed to stop daily application with dithranol for 1 or 2 days if any irritation occurred. If such an interruption in the treatment occurred, patient was instructed to revert to a lower concentration until the next visit. If the maximum concentration of 5% was reached and if no further improvement was seen for at least 2 weeks, the application period was extended to 30 min, 45 min, 60 min or overnight. The treatment was continued until total clearance was reached or a considerable improvement had occurred which was acceptable to the patient.

The second group (10 patients) received the same instructions as to the daily use of dithranol at home. However, the patients were supervised intensively (3 times a week), which permits a faster increase of dithranol concentration. The concentration range of dithranol used in this group was also 0.1%–5%. Each patient in this group started with 3 visits per week until the optimal concentration was reached. From this moment weekly controls were sufficient.

Table I. *Clinical results expressed as the number of patients showing different degrees of relative improvement*

Group 1/w $n=16$, group 3/w $n=10$

Group	<50%	50%–90%	>90%	Drop-out
1/w	4	6	5	1
3/w	1	4	5	0

Clinical evaluation

Once a week, patients of both groups were examined in order to evaluate the clinical result. Scaling, erythema and induration were assessed clinically and scored on a 4-point scale (0–3). In addition, the extent of psoriasis was documented before and after the treatment period. From the percentages of body surface involved and the clinical scores, the Psoriasis Area Severity Index (PASI-score) was calculated (9). In order to express the relative improvement of the individual patient, the following equation was used:

$$\frac{PASI_{before} - PASI_{after}}{PASI_{before}} \times 100\% = \text{relative improvement}$$

The appearance of irritation and staining was monitored on a 3-point scale (−/+/++).

Statistical analysis

Paired and unpaired Wilcoxon ranking tests were used for statistical analysis. *p*-Values less than 0.05 were considered as statistically significant.

RESULTS

The clinical improvement of both groups is summarized in Table I. Group 3/w showed a significantly better results as to the improvement in PASI-score, compared to group 1/w ($p<0.025$).

The duration of treatment periods for both groups is shown in Table II. Both total treatment duration and time required for reaching the optimal concentration are signifiantly longer ($p<0.003$ and $p<0.0001$, respectively) in group 1/w compared to group 3/w. However, the treatment periods of both groups with the optimal concentration were not significantly different.

All patients, except for 3 in group 1/w and 1 in group 3/w, reached high concentrations of dithranol (3%–5%). In 3 patients of group 1/w and 6 patients of group 3/w the application period was extended to 1 hour and overnight application was only necessary in 1 patient of group 3/w. Improvement was enhanced by these extensions.

Table II. *Duration of treatment periods in weeks (means ± SEM)*

t_{tot} = total treatment period; t_{incr} = period for reaching optimal concentration; t_{opt} = period of treatment using optimal concentration

Group	t_{tot}	t_{incr}	t_{opt}
1/w	11.7±1.1	6.7±0.7	4.5±0.6
3/w	7.3±0.8	2.4±0.2	4.9±0.8

Irritation, at concentrations of 1% or more, was seen in 9 of the 16 patients of group 1/w and in 4 of the 10 patients in group 3/w. In group 1/w, 2 patients showed severe irritation. This caused one patient to withdraw from the trial. Although irritation tended to be more frequent and severe in group 1/w, no statistically significant difference was observed compared to the more intensively monitored group. Staining occurred in 2 patients of group 1/w and in 4 patients of group 3/w, all in the last phase of treatment.

DISCUSSION

In the present investigation 33% of the patients seen at weekly intervals cleared compared to a clearing percentage of 50% for the patients seen 3 times a week. Data from the literature amplify the impact of the frequency of control visit. Hindryckx & De Bersaques (10) treated a group of patients at the outpatient clinic according to a similar short-contact dithranol regime, however, with control visits once per 1–3 weeks. These authors reported clearing in only 10% and no effect at all in 35% of the patients. In contrast, a similar short-contact regime carried out at an inpatient department by Paramsothy et al. (11) yielded clearing in 62% of the patients. In the present study clinical improvement, assessed by the difference in PASI-score before and after treatment, proved to be significantly better in group 3/w compared to group 1/w.

Apart from the increased clearing capacity also a shortening of the treatment period was observed in group 3/w. The relatively long period before the optimal concentrations were reached in group 1/w

(6.7 ± 0.7 weeks), is responsible in its own right for the elongated duration of the treatment in this group. Between both groups no significant difference was observed as to the periods of treatment with the optimal concentration of dithranol. Therefore, the initial dose finding phase seems crucial for both treatment duration and clearing capacity.

Although the patients of group 3/w were more prone to irritation due to a higher velocity of concentration increments, the incidence and severity of irritation was more marked in group 1/w. Therefore, intensified controls seem to be essential in order to avoid undesirable irritation. As the maximum irritation of dithranol is observed 48 hours after application (12, 13), dosage increments more frequently than 3 times a week could well result in a high incidence of irritation. Especially in ambulatory patients such should be avoided. Staining proved to be independent of the velocity of concentration adjustments, it rather seems to correlate with extended application times.

Based on the present study, we may conclude that the frequency of control visits is essential in order to achieve an optimal therapeutical effect with high clearing and minimal irritation. It is most essential that patients are well instructed before starting dithranol therapy and that they are prepared for a time-consuming treatment. In this light, an educative attendance at an inpatient department or day-care centre might be a valuable alternative. Anyhow, the first period of treatment requires intensified supervision in order to achieve optimal concentration adjustments and optimal patient compliance.

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