

One-minute Dithranol Therapy in Psoriasis: A Placebo-controlled Paired Comparative Study

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In a double-blind left-right randomised comparison, 27 patients suffering from chronic plaque-type psoriasis vulgaris were treated for one minute with dithranol 2% ointment, Psoralon® (Psoralon MT), on a selected psoriasis plaque on one half of the body and with a placebo ointment on a corresponding plaque on the other. The preparations were applied once daily for 8 weeks. Seventeen patients achieved clearing or considerable improvement with dithranol therapy, as compared with 6 patients with placebo ($p=0.002$). Erythema, infiltration, scaling, pruritus and the overall result were assessed. Statistically significant differences in favour of dithranol treatment were seen for all five variables, except for pruritus. The average of these five variables, designated the mean score, was also analysed; dithranol was seen to yield significantly better results ($p=0.001$). Staining of clothes and the bathroom was noted by 3 and 5 patients, respectively, but no medical side effects were seen. *Key words:* Anthralin; Minute therapy.

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Short-contact dithranol therapy, which could partly eliminate disadvantages, such as staining of clothes and other materials, has gained wide acceptance since the publication of a dithranol penetration study by Schaefer et al (1). Epidermis devoid of the horny layer (a condition comparable with diseased skin) was shown to reach 50 times higher concentrations than normal skin after a 30 min application time. Also, prolongation of the application time from 30 to 1000 min in a state of horny layer disturbance was shown to increase the epidermis concentration by only 50%, in contrast to normal skin, where an increase of 2000% was noted (1).

The objective of the present study was to investigate whether ultra-short (one-minute) contact dithranol therapy has any effect in the treatment of plaque psoriasis. If so, this would further facilitate the use of dithranol, especially for outpatients.

MATERIAL AND METHODS

Subjects

The study comprised 27 outpatients, 21 men and 6 women with a mean age of 45.2 years (SD 14.0 years). The mean total disease duration was 20.5 years (SD 14.8 years) and the duration of the exacerbation 5.1 months (SD 6.4 months). Three of the 30 patients originally entering the study withdrew: one patient's psoriasis deteriorated and he was hospitalised, one patient withdrew after 7 weeks due to alleged lack of efficacy, and one patient was not assessed due to a mistake.

Cooperative patients aged 18-75 suffering from psoriasis vulgaris of the plaque type with bilateral lesions of equal clinical status were included in the study. Informed consent was obtained from all patients. Only patients not having been treated with topical or systemic corticosteroids or subjected to phototherapy 10 days before entry into the study were included.

Material

As the active preparation, Psoralon® 2% ointment (containing 2% dithranol and 2% salicylic acid as a stabilising agent) was used. The placebo ointment contained the same base as Psoralon® but the dithranol was replaced by 1,8-dihydroxyanthraquinone, a yellow substance mimicking dithranol.

Methods

The study was a double-blind left-right randomised comparison.

In each patient, two plaques of equal clinical appearance were selected by the investigator. As a rule, the plaques were located on the elbows or knees. The patients were instructed to apply the preparations on the left or right side of the body on the selected patch (according to randomisation) in a thin layer, and to wash it off after one minute with a soap with low pH. The plaques were then to be treated with an emollient. The patients were provided with pH5-Eucerin® soap and the emollient Unguentum Merck® (Decoderm Basiscreme). UVB phototherapy was initiated by all patients at the same time as entry into the study; the test patches were covered with black UV-blocking plastic material at each treatment session. Thus, no other treatment than the above-described was given to the test patches.

Patients were assessed on entry into the study, after 4 weeks and after 8 weeks of treatment with respect to five efficacy variables: pruritus, erythema, scaling, infiltration and overall result. Each variable was assigned a score: 0 = none, 1 = slight, 2 = moderate and 3 = severe. The degree of clearing was evaluated separately by the physician and the patient on a scale from 0 to 4: 0 = cleared, 1 = considerably improved, 2 = somewhat improved, 3 = unchanged and 4 = deteriorated. Clearing was defined as the absence of erythema, infiltration and scaling.

Statistical analysis

The linear non-parametric permutation test for paired observations (two-tailed) (2) was used to evaluate the difference between treatment groups with respect to each variable.

RESULTS

Statistically significant differences in favour of Psoralon® ointment were seen for all the recorded variables, except for the pruritus score - only 6 patients, however, reported pruritus prior to the study (this number being reduced to one patient posttreatment). The mean mean score and the mean overall result score were 1.9 and 2.5 respectively before treatment. The results are summarised in Table I.

No medical side effects, such as skin irritation, were noted during the study. Three patients complained of staining of clothes and 5 of discolouration of the bathroom.

Table I. Results

Mean score values \pm SEM 8 weeks after treatment with 2% dithranol ointment (Psoralon®) and placebo, respectively

Variable	Psoralon®	Placebo	P-value
Erythema	1.63 \pm 0.13	2.00 \pm 0.14	0.011*
Scaling	0.63 \pm 0.11	0.89 \pm 0.11	0.039*
Infiltration	1.15 \pm 0.14	1.63 \pm 0.13	0.007**
Pruritus	0.07 \pm 0.07	0.07 \pm 0.07	NS
Overall result	1.48 \pm 0.13	1.93 \pm 0.12	0.004**
Mean score	0.99 \pm 0.09	1.30 \pm 0.08	0.001***

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

DISCUSSION

Our study has shown the one-minute treatment with dithranol 2% (Psoralon®) ointment to be superior to placebo for the treatment of chronic plaque psoriasis. The results are not impressive, however, since most previously published studies concerning the efficacy of dithranol have shown better results, even with short-term application. With conventional (classical) dithranol therapy, clearing of 75 to 100% of the patients has been achieved in 11 days to 6 weeks (3–7). The efficacy of short-term application (5–60 minutes) of dithranol has been reported to be excellent (3–6, 8–10); in fact, when comparisons have been undertaken, results equal to (3,5,11) or better than (4–6) those of conventional therapy have been achieved. MacDonald & Marks (9) compared, in a left-right trial, dithranol contact times of 10 minutes and immediate removal (in practice a contact time of 30 s to 3 min.), using 2% dithranol with 0.5% salicylic acid in emulsifying ointment. These two treatment regimens yielded equally good results with a mean clearing time of 21.7 days in 7 out of 8 patients; thus, only one patient failed to clear. Less impressive results similar to those achieved with our one-minute therapy have, however, also been reported. Chlebarov & Rauh (12), using the same preparation as in our study (Psoralon®) but in a 30-day trial, noted slightly better effect of 2% than 1% ointment, even though no statistical analysis was undertaken. They found no difference in efficacy between very short application times (immediate removal) and longer ones (5–10 min). With the use of 2% dithranol, 66% of the patients achieved results which could be classified as "good" (21% cleared and 45% improved considerably). These results are comparable with ours, the corresponding figure being 17/27, i.e. 63%.

The reasons for the somewhat poorer results in the present study can only be a subject for speculation. The concentration of the dithranol may have been too low for such a short application time; this, however, is contradicted by the study of MacDonald & Marks (9). The definition of "clearing" may vary between different trials. A residual erythema is accepted by many investigators but not by us. Finally, the fact that the design of our study – in contrast to many other studies – closely

resembled the way a patient is in fact treated when not participating in a study, i.e. without extensive daily or weekly surveillance and with the treatment being given on an outpatient basis, may also have contributed.

Few of our patients complained of the staining properties of dithranol. This may be explained by the fact that the preparation could be washed off quickly and that only small parts of the body were treated. These two facts may also account for the good patient tolerance, none of the patients experiencing any burning sensation.

In conclusion, the study has confirmed the efficacy of 2% dithranol (Psoralon®) with one-minute application in psoriasis. The application time and the concentration may, however, have to be increased in order to achieve better results.

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