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Comparison of Dithranol and Butantrone in Short Contact Therapy of Psoriasis

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Thirty psoriatic out-patients were treated as a right–left comparison with dithranol (0.1, 0.5, 1, 2%) and butantrone (0.66, 1.3, 2.7, 3.9%) short contact therapy, both in white petrolatum. Fifteen of the treated patients cleared well and no obvious differences between the treated sides were clinically observed. Six patients showed some improvement, but in four of them the dithranol treated side cleared sooner and the therapy was continuted with dithranol short contact therapy on both sides. In two patients the thick lesions cleared slowly and the therapy was continued with dithranol in Lassar's paste. The treatment was discontinued in nine patients: in five patients because short contact therapy was ineffective and in one patient because of strong skin irritation on both treated sides. In three patients the treatment was discontinued for non-medical reasons. Butantrone has an antipsoriatic activity almost equal to that of dithranol. When short contact treatment is used, erythema and staining with butantrone are weaker than with dithranol. Because the short contact tolerability of butantrone was good, it might be possible to start with higher concentrations. *Key word: Anthralin.* (Received July 3, 1986.)

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In spite of the development of new drugs (e.g. psoralens, retinoids), dithranol has maintained an important place in the treatment of psoriasis. Dithranol has been used mainly by in-patients for 24 hours as a stiff paste, because it irritates and stains the skin and clothing. To reduce the side-effects Schaefer et al. (1) introduced the short contact treatment of psoriasis, i.e. dithranol was used in white petrolatum for one hour or less on psoriatic lesions. Further investigations, where short contact treatment was compared with topical steroids (2) and with the Ingram regime (3), showed that short contact therapy is effective in the treatment of psoriasis. Runne & Kunze (4) treated 315 patients with short contact therapy. The therapy was as effective as the traditional dithranol treatment: In 75% of the patients the psoriatic lesions cleared within four weeks. However, irritation of the healthy skin and staining of the skin and clothes have been observed in all short contact trials.

Mustakallio has studied dithranol and related compounds in order to find a derivative of dithranol which would show less staining and irritation while retaining the antipsoriatic properties (5, 6). 10-butyryl dithranol (butantrone) showed experimentally an antipsoriatic effect equal to dithranol (7). When equimolar concentrations of dithranol (0.5%) and butantrone (0.66%) were tested for 20 min or three hours on healthy looking back skin, butantrone caused remarkably less staining and irritation than dithranol (8). Even with higher test concentrations of butantrone (0.66, 2.0, 3.9%) there was no clear increase in either staining or irritation to be seen when short exposures were used (9).

In a pilot study of 37 in-patients (Göransson, unpublished observations) equimolar concentrations of dithranol (0.1, 0.3, 0.5, 1.0%) and butantrone (0.13, 0.39, 0.66, 1.3%) were used on psoriatic lesions for 30 min. Because butantrone in high concentrations did not show any strong irritation when tested (9) and because low concentrations of butantrone seemed to prolong the treatment time, the short contact treatment was started directly in this study with higher concentrations of butantrone.

MATERIAL AND METHODS

Thirty out-patients (19 men and 11 women, mean age 40.5 years, range 16–74 years) with moderate or severe plaque (19 patients), guttate (4 patients) or combined plaque and guttate psoriasis (7 patients) were treated with dithranol and butantrone short contact therapy five times a week. This open trial was approved by the ethical committee of the clinic. The right side of the body was treated with dithranol and the left side with butantrone, both in white petrolatum. On thin lesions the treatment was started with 0.1% dithranol (0.5, 1.0, 2.0%) and 0.66% butantrone (1.3, 2.7, 3.9%). The concentrations were raised every third day of treatment if no irritation was seen. On thick lesions, e.g. on the extensor sides of the limbs, the treatment was started with 0.5% dithranol (1.0, 2.0%) and 1.3% butantrone (2.7, 3.9%). The preparations were applied on the psoriatic lesions for 30 min, thereafter the surplus was removed carefully by patting with soft paper towels and washing with a liquid soap (Lactacyd, pH 3.5). The patients were examined once a week by the author.

The following parameters were observed both visually and by palpation: The scaling and the thickness of the lesions, the irritative erythema of the surrounding skin and the staining of the lesions and surrounding skin (Table I).

If the treatment failed to improve the skin the therapy was discontinued after three weeks. If there was a clear difference to be seen between the dithranol- and butantrone-treated sides, or if clearing of the lesions discontinued after three or four weeks of treatment, the treatment was continued with either dithranol in petrolatum for 30 min on both sides of the body or with dithranol in Lassar's paste for 24 hours.

Statistical analysis was performed using Friedman's two-way analysis of variance within the bodyside. The comparison between the dithranol and butantrone treated sides was performed by using Willcoxon's matched-pairs signed ranks test. Two-sided probability $p<0.05$ was considered statistically significant.

RESULTS

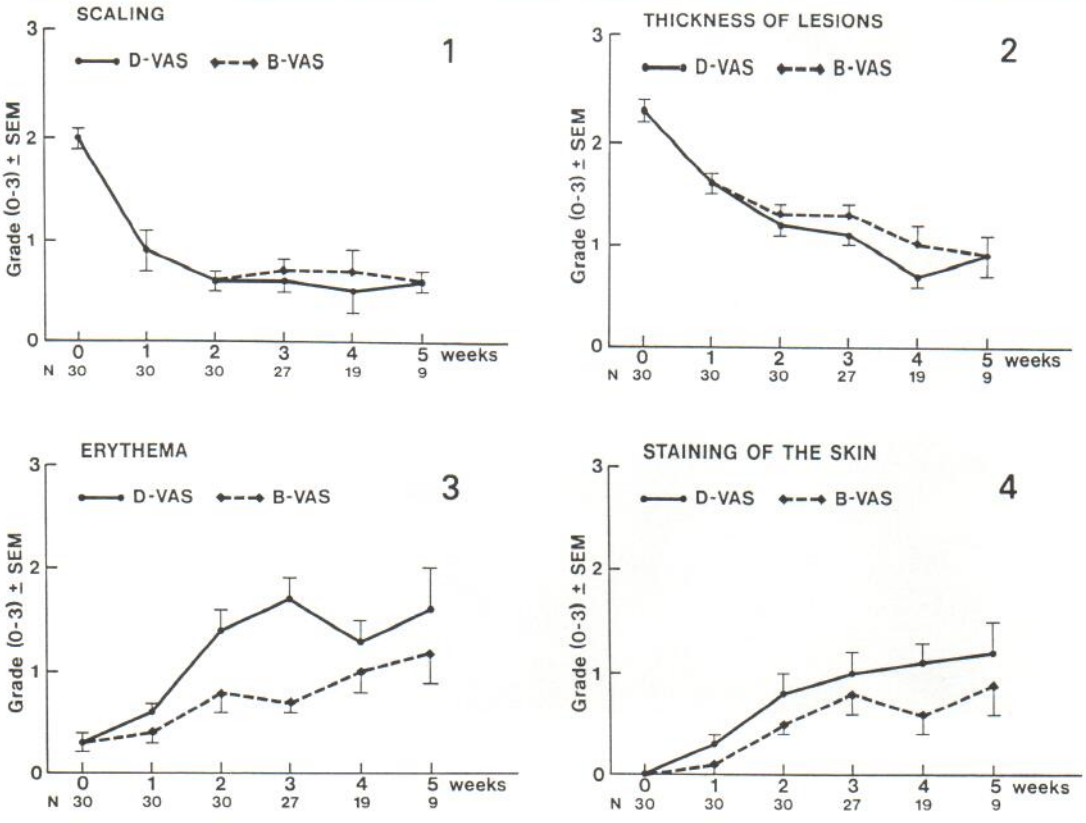
Of the 30 patients studied 15 showed good to excellent (good=80%, excellent= 90%–100% of the lesions were cleared) improvement of the lesions with both dithranol and butantrone short contact therapy. No significant difference in improvement was observed between the treated sides. Six patients showed some improvement with the short contact therapy, however, in two of them the thick lesions cleared slowly compared with the thinner lesions. These were treated with dithranol in Lassar's paste for approximately one week. In four of these patients the dithranol-treated side healed sooner and the treatment was continued with dithranol short contact therapy on both sides of the body.

The treatment was discontinued in nine patients, in five patients because short contact therapy was ineffective and in one patient because of strong skin irritation on both sides of the body after four weeks of treatment. In three patients the treatment was discontinued for non-medical reasons.

Table I. *Clinical evaluation of the psoriatic lesions and the side-effects (erythema and staining) in the surrounding skin*

Scaling	*Thickness of lesions*
3 = profuse	3 = thick
2 = moderate	2 = moderate
1 = thin	1 = thin
0 = no scaling	0 = not palpable
Erythema	*Staining*
3 = intense	3 = dark brown
2 = moderate	2 = reddish brown
1 = faint	1 = brownish hue
0 = no erythema	0 = no staining

If small differences were observed between the treated sides, values of 0.5, 1.5 or 2.5 were also used.



Figs. 1–4. The effects of dithranol (D-VAS) and butanthone (B-VAS) on scaling (Fig. 1) and thickeness (Fig. 2) of the lesions and on erythema (Fig. 3) and staining (Fig. 4) the surrounding skin. *N*=the number of patients.

The scaling of the lesions (Fig. 1) decreased similarly on both dithranol- and butantrone-treated sides. Butantrone caused a slight rise in scaling after three weeks of treatment, but this was not statistically significant.

The thickness of the lesions (Fig. 2) cleared on the dithranol-treated side sooner compared with the butantrone-treated side. The difference was statistically significant on the second week ($p<0.05$), third week ($p>0.02$) and on the fourth week ($p>0.01$) of treatment.

The erythema (Fig. 3) of the surrounding skin appeared sooner on the dithranol-treated side and was more intensive than the erythema caused by butantrone. The difference was statistically significant on the second ($p<0.01$) and third week ($p<0.01$) of treatment.

The staining (Fig. 4) of lesions and the surrounding skin was seen on the dithranol-treated side after two weeks of treatment. The staining on the butantrone-treated sides developed after three weeks of treatment and was weaker than on those treated with dithranol. The differences were statistically significant after one week, two weeks and four weeks of treatment ($p<0.05$).

DISCUSSION

Before this comparative short contact study was started, two clinical trials with butantrone have been performed both using a paraffin stick formulation overnight. The first study (10)

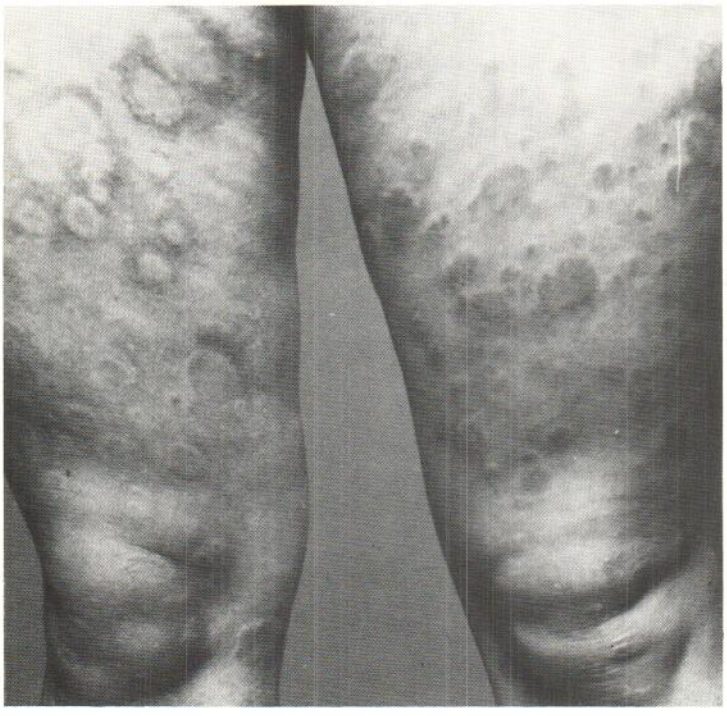


Fig. 5. A 34-year-old woman treated with short contact therapy for three weeks. The dithranol-treated side shows remarkable irritation.

was done with 30 out-patients as an open right–left comparison. Dithranol was used as a 3% paraffin stick and butantrone was used in an equimolar concentration (4%) also in a paraffin stick overnight. Ten patients (33.3%) discontinued the treatment because of skin irritation. Six of these patients got irritation of both dithranol and butantrone, four tolerated better dithranol. One patient could not use dithranol (Fig. 5), but cleared with butantrone. The antipsoriatic activity of the drugs was equal but staining was markedly milder with butantrone. The irritation caused by butantrone reached its maximum after six to ten weeks.

In an uncontrolled multicenter study (10) butantrone was used alone as a 4% paraffin stick daily overnight on psoriatic lesions. Of the 141 out-patients treated 39 (28%) got marked irritation and six patients had to be treated in hospital. Two of them got fever and leukocytosis. The irritation of butantrone appeared usually after four to eight weeks of treatment. This delayed irritation may be due to a cumulative effect of butantrone, because its oxidative inactivation is slower than that of dithranol (11).

The short contact modality was chosen for the present clinical trial because the removal of the surplus drug before it has penetrated the healthy looking skin might prevent the accumulation of butantrone. Moreover, tape stripping experiments (8, 9) have shown that butantrone exposures shorter than one hour caused no staining and seldom, if ever, a disturbing erythema.

During the short contact therapy psoriatic lesions on the dithranol-treated side generally cleared sooner than those of the butantrone-treated side. Clinically the differences were not very significant except in four patients, in whom the treatment was continued with dithranol short contact therapy on both sides of the body. The irritation of the healthy skin appeared later on the butantrone-treated side and was weaker than that caused by dithranol.

In this study no systemic side-effects were observed in any of the patients treated. Only in one patient the treatment had to be interrupted because of marked irritation on both dithranol- and butantrone-treated sides. The best results were seen in patients with thin and small psoriatic lesions, whereas large and thick lesions healed more slowly.

A similar short contact study with 37 patients was done recently in Germany as a multicenter investigation (Molz & Brandt, personal communication). Dithranol (0.1, 0.5, 1.0%) and butantrone (1.3, 2.7, 3.9%) were used as a double blind right-left comparison, both in white petrolatum. The results revealed no clear difference in the antipsoriatic effect of the two drugs, but, compared with dithranol, irritation and staining of the surrounding skin was less with butantrone.

The short contact butantrone therapy is a practical form of treatment for out-patients, although it needs supervision by a physician and a cooperative patient to succeed. In the present study the treatment was given five times a week. If the therapy was irregular, especially during the first two weeks of treatment, there was a relapse to be seen and the time of clearing was prolonged.

As a conclusion, butantrone has an antipsoriatic activity almost equal to that of dithranol. When the short contact regime is used, the side-effects (erythema and staining) are weaker with butantrone than with dithranol. In a previous study (9), where different concentrations of butantrone (0.66, 2.0, 3.9%) were tested for 20 min or one hour, no remarkable difference in irritation was observed between the concentrations. Therefore it should be possible to use only one rather high concentration of butantrone in short contact therapy instead of a gradual increase in concentration.

REFERENCES

1. Schaefer H, Farber EM, Goldberg K, Schalla W. Limited application period for dithranol in psoriasis. Preliminary report on penetration and clinical efficacy. Br J Dermatol 1980; 102: 571–573.
2. Lowe NJ, Ashton RE, Kouds H, Vershoore M, Schaefer H. Anthralin for psoriasis: Short-contact anthralin therapy compared with topical steroid and conventional anthralin. J Am Acad Dermatol 1984; 10: 69–72.
3. Statham BN, Ryatt KS, Rowell NR. Short-contact dithranol therapy. A comparison with the Ingram regime. Br J Dermatol 1984; 10: 703–708.
4. Runne U, Kunze J. Die "Minutentherapie" der Psoriasis mit Dithranol und ihre Modifikationen. Hautartzt 1985; 36: 40–46.
5. Mustakallio KK. Irritation and staining by dithranol (anthralin) and related compounds. I. Estimation with chamber testing and contact thermography. Acta Derm Venereol (Stockh) 1979; 59 (Suppl 85): 125–132.
6. Mustakallio KK. Irritation and staining by dithranol (anthralin) and related compounds. II. Structure-activity relationships among 10-meso-substituted acyl analogues. Acta Derm Venereol (Stockh) 1980; 60: 169–172.
7. Mustakallio KK, Brandt H. Antipsoriatic activity of 10-acyl analogues of dithranol (anthralin). I. Phase I clinical trial of 10-propionyl dithranol and 10-butyryl dithranol (butantrone). Acta Derm Venereol (Stockh) 1984; 64: 63–66.
8. Göransson A, Kolari PJ, Mustakallio KK. Irritation and staining by dithranol (anthralin) and related compounds. V. Short-contact and tape stripping experiments with dithranol and butantrone. Acta Derm Venerol (Stockh) 1984; 64: 134–139.
9. Göransson A. Irritation and staining by dithranol (anthralin) and butantrone (10-butyryl dithranol). Further short contact and tape stripping experiments. Acta Derm Venereol 1987; 67: 72–76.
10. Brandt H. Antipsoriatic activity of 10-acyl analogues of dithranol (anthralin). II. Clinical comparison of dithranol and butantrone sticks with special reference to side effects. Acta Derm Venereol (Stockh) 1987; 67: 55–61.
11. Taskinen J, Haarala J, Wartiovaara E, Halmekoski J. Oxidation of antipsoriatic 10-acyldithranol derivatives to 1,8-dihydroxyanthraquinone. In: FIP-85 Abstracts. 45th International Congress of Pharmaceutical Sciences, Montreal, 1985; 225.