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Short-contact Therapy for Psoriasis with 3.9% Butantrone (10-Butyryl Dithranol)

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Previous studies have shown that when butantrone and dithranol were used in equimolar gradually increasing concentrations in short-contact therapy for psoriasis the efficacy of butantrone was somewhat lower compared to dithranol. To see whether the efficacy of butantrone in short-contact therapy could be increased by starting with a single high-concentration directly, 20 psoriatic patients were treated with dithranol (0.1,–0.5,–1.0,–2.0%) and butantrone (3.9%) short-contact therapy as a right-left comparison. With these treatment modalities the antipsoriatic effects of dithranol and butantrone were similar. Although the efficacy of 3.9% butantrone was better than the previously used butantrone therapy with gradually increasing doses, there was a parallel increase in side-effects. In general, the side-effects (erythema and staining) remained weaker on the butantrone-treated side than on the dithranol-treated side. No systemic adverse-effects were observed in any of the treated patients. *Key word: Anthralin.*

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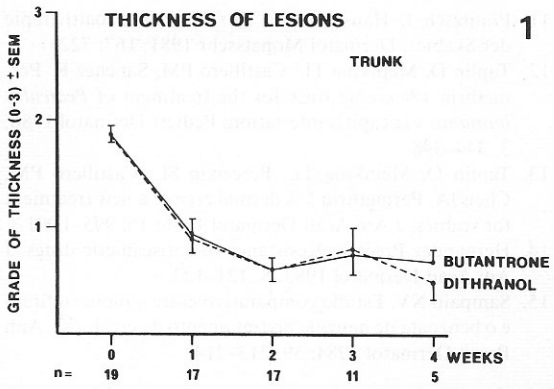
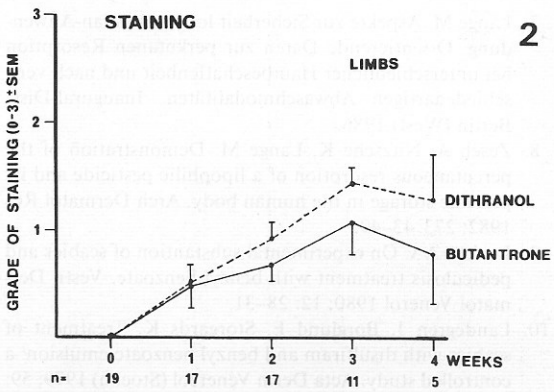
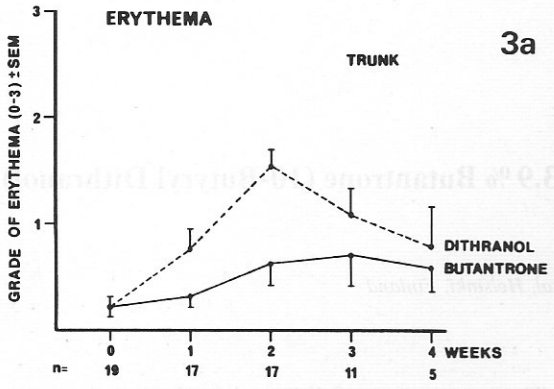
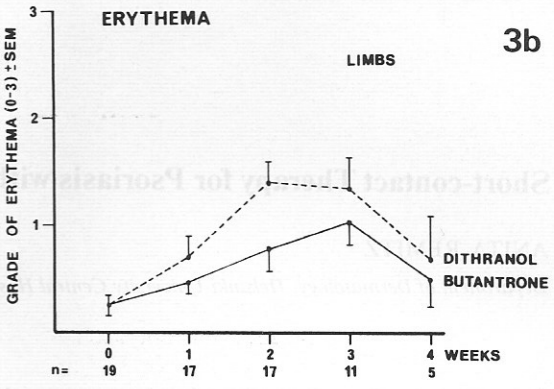
The introduction of dithranol (anthralin) short-contact therapy for psoriasis (1) has made it also possible to use dithranol in the treatment of out-patients, and even home-patients. The major problems with dithranol therapy, even when short-contact therapy has been used, have been irritation of the surrounding healthy-looking skin, and to a lesser extent the staining of skin, clothes, bathtubs and shower basins. Mustakallio tried to reduce the side-effects by designing derivatives of dithranol with similar antipsoriatic properties as dithranol but which produced less irritation and staining. In experimental studies 10-butyryl dithranol (butantrone) seemed to meet these criteria best (2, 3).

When butantrone (0.66, 1.3, 2.0 and 3.9%) was used in the treatment of psoriasis patients as a right-left comparison with dithranol (0.1–0.5, 1.0 and 2.0%) in short-contact therapy for 30 min, butantrone was almost as effective as dithranol in the treatment of psoriasis but less irritation was observed (4). The present study was designed to see if 3.9% butantrone could be used directly in short-contact therapy without increasing the side-effects. The effect of 3.9% butantrone was compared with regular dithranol treatment in short-contact therapy.









Figs. 1–3. Changes in thickness of lesions (Fig. 1), staining of the surrounding skin (Fig. 2) and erythema of the surrounding skin (Figs. 3 *a* and 3 *b*), during four weeks of short-contact therapy with dithranol or butantrone. *N* = number of patients.

MATERIAL AND METHODS

Twenty patients (14 men and 6 women, mean age 46.3 years, range 21–75 years) with moderate to severe plaque or guttate psoriasis were treated with dithranol (0.1, 0.5, 1.0 and 2.0%) on the right side of the body and with 3.9% butantrone on the left side of the body, both in white petrolatum, six times a week for four weeks as short-contact therapy. The surplus was removed after 30 min as described earlier (4). The concentrations on the dithranol-treated side were increased every third day if no irritation was observed. Three of the patients had psoriasis of the guttate type and seventeen of the plaque type. The patients were monitored weekly and the following parameters observed: thickness of the lesions (3= thick, 2= moderate, 1= thin, 0= not palpable), scaling of the lesions (3= profuse, 2= moderate, 1= thin, 0= no scaling), irritative erythema of the surrounding skin (3= intense, 2= moderate, 1= faint, 0= no erythema) and staining of the skin (3= dark brown, 2= reddish brown, 1= brownish hue, 0= no staining). If small differences between the treated sides were observed, values of 0.5, 1.5 and 2.5 were used.

The statistical method used for comparison of the dithranol- and butantrone-treated sides was Wilcoxon's matched pairs signed ranks test. Two-sided probability $p<0.05$ was considered statistically significant.

RESULTS

Of the 20 treated patients, eleven (55%) cleared up well or excellently (80–100% of the lesions) within 4 weeks. Two patients experienced some relief with both dithranol and butantrone short-contact therapy, but the response was slow. In seven patients (35%) the therapy was discontinued: In four patients (20%) because of irritation of the perilesional skin; two had more irritation on the butantrone-treated side, one on the dithranol-treated side and one on both sides of the body. One of these patients had irritation on the butantrone-treated side after the first treatment. After a few days he developed a pustular eruption, first on the left lower limb (the butantrone-treated side) and later also on the right lower limb (the dithranol-treated side). Contact allergy was excluded by epicutaneous testing. The values for this patient were excluded from the figures because the treatment was stopped before the first control (one week). No systemic side-effects were observed in any of the patients.

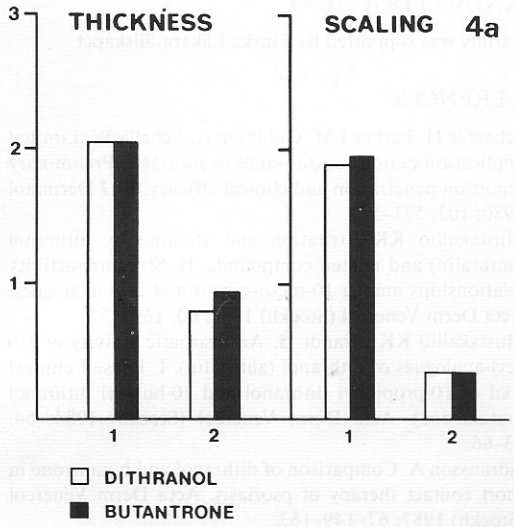


Fig. 4. The paragrams show the mean values for the patients at the beginning of the therapy and at the end of the therapy.

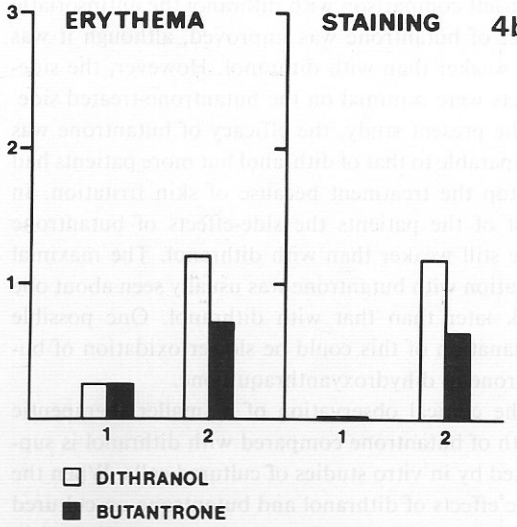


Fig. 4 *a* shows the lesional parameters and Fig. 4 *b* the perilesional side-effects. 1 = baseline, 2 = end of treatment.

In two patients the therapy was interrupted because of slow response to the therapy; in one patient the improvement of psoriasis on the butantrone-treated side was slower than that on the dithranol-treated side. In the other patient, both sides cleared slowly and the treatment was changed to dithranol in Lassar's paste. One patient interrupted the study for non-medical reasons.

The changes in the thickness of the lesions, irritative erythema and staining are shown in Fig. 1–3. The reductions in the thickness of the lesions and scaling showed no statistically significant differences between the dithranol- and butantrone-treated sides, therefore only the reduction in thickness of the trunk lesions is shown in Fig. 1. The lesions on the trunk cleared more rapidly than on the limbs.

The irritative erythema was more pronounced on the dithranol-treated side after two weeks of treatment ($p<0.01$) but after four weeks statistically significant changes were no longer observed. The staining was stronger on the dithranol-treated side after three and four weeks of treatment, but the differences were not statistically significant. The mean short-contact treatment time was 2.45 weeks. The values after the third and fourth week were difficult to interpret because the total number of patients had diminished (3 weeks, $n=11$; 4 weeks, $n=6$) due to differences in clearing of the lesions. Therefore, the mean values at the beginning and end of the treatment are shown in Fig. 4. These values show that the staining of the dithranol-treated side is stronger ($p<0.01$) at the end of the treatment compared to that with butantrone, although the weekly values show no statistically significant differences. The erythema on the dithranol-treated side at the end of the treatment was also more pronounced ($p<0.05$) compared to that with butantrone.

DISCUSSION

The short-contact regimen was chosen for this study because of previous reports of delayed irritation when 4% butantrone paraffin stick was used overnight (5). Also Greaves observed irritation when 0.5 and 1% butantrone was used in white soft paraffin overnight (6). Both dithranol and butantrone are decomposed to 1, 8-dihydroxyanthraquinone but dithranol is decomposed more rapidly (7). This can lead to a cumulation of the more slowly oxidizable butantrone in tissues and cause the delayed irritation which was observed.

Previous studies have revealed that when equimolar concentrations of dithranol and butantrone were used in short-contact therapy, the lower concentrations of butantrone were ineffective (Remitz, unpublished). When comparably higher concentrations (0.66, 2.7 and 3.9%) of butantrone were used (4) in a

right-left comparison with dithranol the antipsoriatic effect of butantrone was improved, although it was still weaker than with dithranol. However, the side-effects were minimal on the butantrone-treated side. In the present study, the efficacy of butantrone was comparable to that of dithranol but more patients had to stop the treatment because of skin irritation. In most of the patients the side-effects of butantrone were still weaker than with dithranol. The maximal irritation with butantrone was usually seen about one week later than that with dithranol. One possible explanation of this could be slower oxidation of butantrone to dihydroxyanthraquinone.

The clinical observation of a smaller therapeutic width of butantrone compared with dithranol is supported by in vitro studies of cultured cells. When the toxic effects of dithranol and butantrone on cultured keratinocytes (8) or HeLa cells (9) were studied, dithranol showed a linear dose-dependent decrease in the number of viable cells, whereas equimolar concentrations of butantrone had no effect on cell numbers at low concentrations but the highest concentration (10^{-5} M) showed an abrupt decrease in cell numbers, which was stronger than that with dithranol.

Because of previous reports of delayed irritation in overnight treatment with butantrone (5) it would be recommended to limit the treatment times with butantrone even in short-contact therapy to one month to avoid the delayed cumulative irritant effects of butantrone. Used in such a way, butantrone could be an alternative to dithranol treatment, and especially to some of those patients who cannot tolerate dithranol.

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