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Clobetasol propionate ointment compared with dithranol in Lassar's paste in the treatment of psoriasis

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SUMMARY

The initial results on ten patients in a trial of clobetasol propionate (Dermovate) ointment compared with dithranol in Lassar's paste are described. The rates of clearing for each preparation in each patient were not noticeably different. Relapse was slower with clobetasol propionate in all but one patient for whom there was no preference. The results are highly significant ($P<0.005$).

Psoriasis is a common chronic skin disease. At St Bartholomew's Hospital it accounted for 8·6% of new referrals to the out-patient's department in the first 6 months of 1975 as compared with 19% for warts, 15% for eczema, 4% for urticaria and 3% for all skin tumours. It is a condition characterized by long relapses and spontaneous remissions and accounts for a much higher proportion of out-patient follow-ups.

Such chronic conditions are the subject of numerous and diverse treatments which underline the lack of a cure or a perfect system of management. This is certainly true of psoriasis for which numerous topical and several systemic antimitotic agents are currently in use.

Cell poisons such as arsenic, mercury, resorcin and chrysarobin not only work in theory but have been used successfully in practice (MacKenna, 1959); similarly superficial radiotherapy is useful. However, their side-effects outweigh their usefulness. Current local regimens include ultraviolet light, topical dithranol, salicylic acid, coal tar fractions and the more potent steroids, while systemic regimens employ azathioprine, methotrexate and more recently azarabine (Keefer, Roenigk & Hawk, 1975) and, more rarely, systemic corticosteroids such as triamcinolone.

All but a small minority of patients respond promptly over 10–21 days to intensive in-patient treatment with coal tar baths, minimal erythema doses of ultraviolet light and twice daily applications of 0·05–2·5% dithranol in Lassar's paste. Modifications of this type of regime have been described by Ingram (1954) and Seville (1966).

The messiness of coal tar preparations and the staining and irritation of dithranol preparations with damage to clothes and the time necessary in executing therapy are often a deterrent to their effective out-patient use. When the staining and irritating properties of dithranol are modified and lessened a large part of the therapeutic efficacy is lost (Hellier & Whitefield, 1967; Hodgson & Hell, 1970).

The availability of topical halogenated steroids, for example triamcinolone, was welcomed as a major therapeutic advance. Later modifications such as the addition of water-soluble vitamin A were noted to increase their efficacy still further (Jarrett & Spearman, 1965). Odourless non-staining preparations rapidly cleared psoriatic lesions. Subsequently fluocinolone acetonide and betamethasone valerate became available topically but they brought about suppression of psoriatic lesions rather than permanent resolution. When therapy with these agents is stopped rapid relapse occurs while prolonged application leads to skin atrophy, telangiectasia and also to the skin lesions becoming refractory to further treatment.

Studies of the comparative effectiveness of topical corticosteroids and dithranol have given conflicting results. Knudsen (1965) noted that using fluocinolone, relapse occurred more rapidly than with conventional dithranol treatment, whereas Juhlin (1968) and Suurmond (1968) found evidence to the contrary.

The introduction of clobetasol propionate in a strength of 0·05% in the treatment of psoriasis suggested more rapid clearing of psoriatic lesions. In a double-blind study it was shown to be superior to other topical steroids in the treatment of psoriasis (Sparkes & Wilson, 1974).

Munro & Pringle (1975) have demonstrated, in a small group of cases, that clobetasol propionate ointment with or without added dithranol is as effective as is Lassar's paste with dithranol, and patients so treated tended to have longer periods of remission. The present trial was carried out to establish whether intermittent treatment with clobetasol propionate ointment is superior to conventional dithranol in Lassar's paste in the treatment of psoriasis.

MATERIALS AND METHODS

Patients with troublesome untreated symmetrical plaque psoriasis were admitted to the ward for intensive treatment in the trial. The preparations used were clobetasol propionate 0·05% in an ointment base (Dermovate) and 0·25% dithranol in zinc and salicylic acid paste B.P. (Lassar's paste) prepared in the St Bartholomew's Hospital pharmacy. A lower concentration of dithranol was used in some patients in whom the higher strength caused irritation.

Having been admitted the patients were examined and the type and distribution of their psoriasis recorded. The nature of the trial and of the ointments involved was explained to each patient before the trial. Treatment with twice daily applications by nurses of clobetasol propionate ointment to the lesions on the right side of the body and dithranol paste to the lesions on the left was begun on day 1 (Fig. 1). Scalp psoriasis was excluded from the trial and treatment. The treated skin was examined daily and the day of complete clearing of all lesions noted and recorded for each side.

On discharge, patients were instructed to use no local treatment but to make a careful note of the day on which psoriasis recurred on each side. The first follow-up appointment was 3 weeks after leaving hospital. The length of remission was taken as an index of the efficacy of each drug.

RESULTS

So far seventeen patients have entered the trial. Two have been lost to follow-up. In one patient, a 16-year-old boy with total body psoriasis, treatment had to be discontinued after 8 days when he entered a pustular phase requiring methotrexate.

The results of the first ten completed patients are recorded in Tables 1 and 2. All patients required between 10 and 21 days to clear their psoriasis and in only one patient, V.L., was there noticeable difference in the rate of clearing of the two sides.

Apart from patient C.C., in whom the psoriasis recurred simultaneously on the two sides, the skin

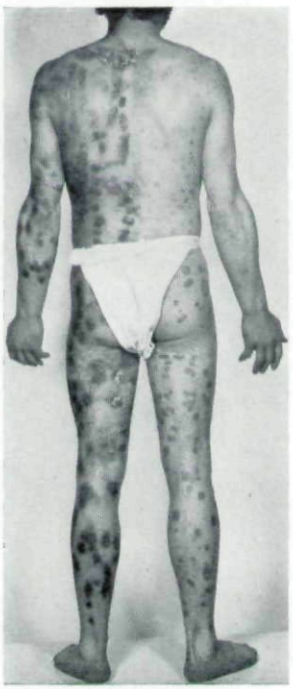

FIGURE 1. Patient treated with Dermovate ointment on right side and dithranol paste on his left.

TABLE 1. Length of treatment until clearance of all lesions (in days) for the first ten patients

Patient	Time for clearance (days)	
	Clobetasol	Dithranol
C.C.	14	14
J.D.	11	11
P.F.	18	18
R.J.	14	14
D.N.	10	10
V.L.	21	18
B.M.	16	16
L.O.	15	15
K.S.	14	14
F.W.	17	17

TABLE 2. Length of remission (in days) and treatment preference in first ten patients

Patient	Days clear after discharge		Preference	
	Clobetasol	Dithranol	Clobetasol	Dithranol
C.C.	11	11	o	o
J.D.	12	5	+	–
P.F.	8	1	+	–
R.J.	21	7	+	–
D.N.	18	15	+	–
V.L.	48	43	+	–
B.M.	22	14	+	–
L.O.	45	14	+	–
K.S.	14	7	+	–
F.W.	34	13	+	–

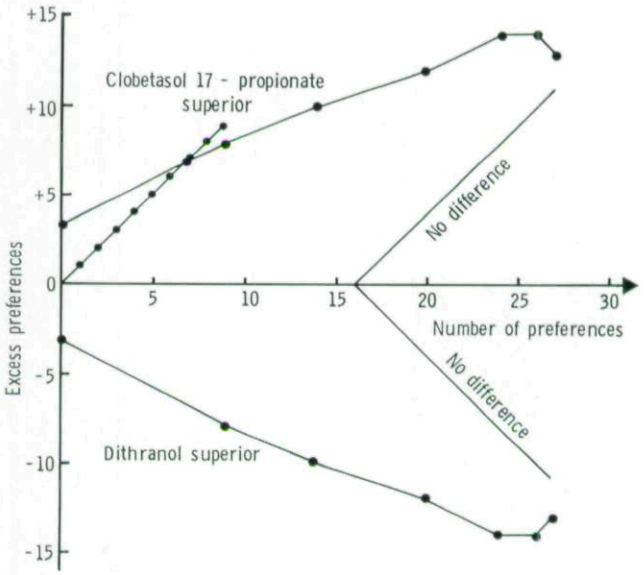

FIGURE 2. Sequential analysis showing seven consecutive preferences for Dermovate-treated side. Restricted sequential analysis $O = 0{\cdot}85$; $2\alpha = 0{\cdot}05$; $1-\beta = 0{\cdot}95$.

remained clear longer on the clobetasol-treated side in all patients (mean 23·3 days, ±s.d. 14·1) compared to the dithranol-treated side (mean 13·0 days, ±s.d. 11·5).

Armitage's (1960) method of restricted sequential analysis lends itself especially for use in trials involving small numbers of patients. The method ignores those who react equally ('tied pairs'). A design corresponding to a 5% level of significance was chosen (Fig. 2) and the clobetasol propionate boundary was reached when the seventh patient had completed the trial.

An alternative method of analysis described by Siegel (1956) does not employ sequential recording. Using this 'sign test' the hypothesis that there is no difference between the two preparations can be

rejected in favour of the alternative hypothesis that there is a difference at the 0·5% significance level. In this investigation all preferences for the length of remission are for clobetasol propionate ($P<0{\cdot}005$).

DISCUSSION

Psoriasis is a disease of remission and relapse. The course varies from patient to patient and at different times in the same patient. The advantage of the method used in this trial is that two treatments can be compared simultaneously. The very nature of dithranol, its staining and irritating action on the skin and its preparation in paste, precludes the use of a double-blind trial, when comparing it with clobetasol propionate ointment.

Table 1 suggests that clobetasol propionate ointment and dithranol in Lassar's paste produce equally satisfactory clearance of psoriasis over a similar time course. However, Table 2 shows a wide variation in the periods of remission induced by each preparation.

The mean remission rates have wide standard deviations. This may well reflect the nature of the disease in individual patients. With such a variation, selection of a patient with a remission differing greatly from the others could distort the mean and invalidate any conclusion drawn. By observing the behaviour of a patient's skin to the simultaneous use of two treatments establishing a 'preference' for one or other treatment and by the use of appropriate methods of statistical analysis these difficulties can be overcome.

Although at the beginning of this trial we selected 0·25% concentration of dithranol some patients experienced irritation. The concentration was reduced stepwise until this effect was overcome. We do not feel this invalidates the trial but rather that some patients who are more sensitive to dithranol react and respond at a lower dose. It could be argued that the right side of the body behaves intrinsically differently from the left. The trial continues at present with the sides of application reversed.

Although the present study is small the result is highly significant. We have shown clobetasol propionate to be superior to dithranol. It is preferred by patients for its cosmetic properties, absence of irritation and staining. If used intermittently in this way and with proper supervision, the atrophic effects seen with continuous therapy should be less. Thus it may have an important part to play in out-patient management of psoriatic patients in the future.

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DISCUSSION

DR G.HOLTI (NEWCASTLE): Topical applications are the only drugs in which the dosage is not specified by the prescribing doctor and more attention will have to be paid to this in the future. I find it perfectly acceptable to use potent corticosteroids such as Dermovate provided they clear an attack of psoriasis completely within 3 weeks, and are not used for a longer period.

DR P.J.MARRIOTT: I agree. If I am treating patients in out-patients with Dermovate, I always like to see them every fortnight and not every 3 months or so.

DR A.B.SHRANK (SHREWSBURY): I think it falls on the pharmaceutical companies to make it clear to the general practitioner and to the patient what sort of quantities are required for lesions.

DR E.S.SNELL (LONDON): The pharmaceutical companies have far less control over doses for patients than the doctor. It is the doctor prescribing it who has the greatest control over the dosage the patient receives. Dermovate is a steroid which has side effects and has to be used very carefully. The best source of information on this is the Data Sheet which we supply.