

## INVESTIGATION OF POSSIBLE DOSAGE REGIMENS FOR TOPICAL STEROIDS USING THE VASOCONSTRICTOR ASSAY

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Psoriatic patients may become resistant to topical steroids after repeated application. Such tachyphylaxis has also been demonstrated in the vasoconstrictor assay, with considerable recovery occurring if a "rest period" intervenes in the dosage regimen (du Vivier & Stoughton 1975; Barry & Woodford 1977). Lack of clinical studies comparing the use of potent topical steroids in twice daily, daily and alternate-day regimens (Cornell & Stoughton 1980) prompted investigation of such regimens in the repeated-application vasoconstrictor test.

5 mg of each preparation (amcinonide cream 0.1%, ditto 0.025%, amcinonide ointment 0.1%, Betnovate cream) were rubbed (1 min) into 7 x 7 mm areas on each forearm of ten volunteers. On the first day each formulation was applied thrice, thence twice daily, once daily or once on alternate days for 4 days. No corticosteroids were applied on days 6 and 7 but on days 8-12 the procedures were repeated, omitting the thrice-daily "loading dose" on day 8. Blanching was estimated in a double-blind manner using a 0-4 scale with half-point ratings for intermediate readings immediately before reapplication and at additional times to provide 55 results for each formulation/regimen up to 373 hours after initial application.

Variance analysis of blanching data as "square root transformation" followed by calculation of the minimum significant range value (Barry & Woodford 1974) permitted statistical comparison of formulations/regimens (Table 1).

Table 1. Blanching response to each preparation in each regimen

<sup>a</sup> Preparation, regimen	<sup>b</sup> Area under curve % x hr	<sup>c</sup> T <sub>m</sub> /10 mean value	Preparation, regimen	Area under curve % x hr	T <sub>m</sub> /10 mean value
HC/A	7580	9.77	LC/B	5230	8.07
HC/B	6170	8.84	LC/A	4980	7.90
HC/C	5260	8.20	LC/C	3920	6.97
O/A	6210	8.84	BV/B	4870	7.78
O/B	5750	8.46	BV/A	4130	7.10
O/C	5040	7.86	BV/C	3840	6.76

a HC, amcinonide cream 0.1%; LC, ditto 0.025%; O, amcinonide ointment 0.1%; BV, Betnovate cream; A, daily application; B, twice daily; C, alternate day.

b From planimetry of % total possible score-time (hr) blanching profile.

c Sq root transformation sum of scores (T<sub>m</sub>) divided by no. of volunteers (10); minimum significant range value  $k = 1.53$  ( $P = 0.05$ ) i.e. if T<sub>m</sub>/10 values differ by more than 1.53 there is significant difference between preparations/regimens.

The blanching effectiveness rank order was daily > twice daily > alternate day application (very potent formulations) and twice daily > daily > alternate day (potent preparations). Results suggest the once-daily regimen should be preferred clinically because a) it was the only one allowing statistical differentiation between formulations eg. amcinonide cream 0.1% was significantly more potent ( $P = 0.05$ ) than ditto 0.025% and Betnovate cream, confirming potency classifications obtained previously (Woodford & Barry 1977; Woodford & Haigh 1979), b) patient compliance should be facilitated, c) less total steroid would be applied.

Barry, B.W., Woodford, R. (1974) *Br.J.Dermatol.* 91: 323-338

Barry, B.W., Woodford, R. (1977) *Ibid.* 97: 555-560

Cornell, R.C., Stoughton, R.B. (1980) *Pharmac.Ther.* 11: 497-508

du Vivier, A., Stoughton, R.B. (1975) *Arch.Dermatol.* 111: 581-583

Woodford, R., Barry, B.W. (1977) *Curr.Therap.Res.* 21: 877-886

Woodford, R., Haigh, J.M. (1979) *Ibid.* 26: 301-310