EFFECTS OF PHOSPHATIDYLCHOLINE ON TOPICAL CORTICOSTEROID BIOAVAILABILITY IN-VIVO

M. Jacobs, G.P. Martin, C. Marriott, Department of Pharmacy, Brighton Polytechnic, Moulsecoomb, Brighton BN2 4GJ

Improved disposition of corticosteroids within the skin layers has been claimed following the topical application of a preparation containing triamcinolone acetonide incorporated into liposomes (Mezei & Gulasekharam 1980). However, the direct effect of phospholipid application to intact skin upon drug absorption has not previously been investigated. The purpose of this study was to examine the effects of pre-treating skin with phosphatidylcholine (PC) on the bioavailability of four proprietary corticosteroid formulations.

Vasoconstrictor activities of Dioderm®, Eumovate®, Betnovate® and Dermovate® creams were assessed using a non-occluded multiple dosage regimen. Aliquots of a liposomal suspension (0.5 ml) containing 5 mg ml^{-1} PC were rubbed into the flexor surface of the 'test' forearms twice daily for 7 days in 10 subjects prior to any steroid application. Buffer was similarly applied to the 'control' arms. Twice daily treatment was maintained for 2 weeks with the application being not less than 1 hour previous to that of any steroid. 5 $\pm$ 1 mg of each steroid formulation was applied to two 7 x 7 mm square areas on each forearm. The preparations were applied twice (0 and 6 h) on day 1 to provide a loading dose and then once daily (9.00 - 10.00 h) on days 2 - 5. No corticosteroids were applied on days 6 and 7 but commencing on day 8, the 5-day application procedure was repeated. Estimation of pallor was made over the 2 week period using a 0 - 4 scale with half-point ratings (Barry & Woodford 1974).

The combined results of all four preparations were then summed for all subjects at each time and expressed as a percentage of the total possible score (% TPS), one of the parameters which is indicative of topical bioavailability (Barry & Woodford 1974). Differences between the daily peak responses obtained from PC treated (T) and control arms (C) are shown in the Table. The blanching response on the control arm was greatest on day 2, diminishing over the following 3 days due to tachyphylaxis, as previously reported (Barry & Woodford 1977). The PC treated arms also attained the highest peak on day 2 but failed to exhibit any perceptible tachyphylactic response over days 3 - 5. The diverging profiles are reflected by the increased differences in peak response values over the first week (Table). On days 4 and 5 the peak response values between control and test arms become significantly different. Results for week 2 follow a similar pattern to week 1 and although tachyphylaxis became evident on the PC treated arms differences between the blanching response on the two arms were significant on days 9 - 12.

Table Peak blanching responses (% TPS) induced by multiple steroid applications

Day:	1	2	3	4	5	8	9	10	11	12
					(% TPS)					
T	27.5	34.5	32.2	34.2	31.4	34.2	41.3	37.2	33.6	34.7
C	26.1	29.8	26.1	23.1	20.0	30.8	31.7	26.7	25.2	25.5
T - C	·1.4	4.7	6.1	11.1**	11.4*	3.4	9.6**	10.5**	8.4**	9.2**

*$p < 0.05$, **$p < 0.01$ using a 2-tailed t-test

The total lipid content of the stratum corneum may have increased following PC treatment enabling a depot of steroid to be formed, leading to a more controlled delivery to the lower skin layers and a reduced tachyphylactic response.

Mezei, M., Gulasekharam, V. (1980) Life Sciences 26: 1473-1477
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