Rapid Assay of the Anti-inflammatory Activity of Topical Corticosteroids by Inhibition of a UVA-induced Neutrophil Infiltration in Hairless Mouse Skin

II. Assessment of Name Brand versus Generic Potency

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The hairless mouse model of a UVA-induced dermal neutrophilic infiltrate was used to compare the efficacy of equal concentrations of name brand versus generic corticosteroids. The generic brand was significantly less effective in suppressing the inflammatory response.

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Within the last decade there has been over a five-fold increase in the United States in the number of generic products reaching the market (1). With regard to corticosteroids, serious questions have been posed about the equivalence of generic products in comparison to the name brand (1-3). A number of studies have put the question to test using the human vasoconstriction assay (4-6). In two studies (5, 6) the generic betamethasone dipropionate was found to be less potent than the name brand. A similar discrepancy was found with betamethasone valerate preparations (6). Interestingly, Stoughion (4) found no difference between three concentrations (0.025, 0.1, 0.5) of Kenalog® cream (triamcinolone acetonide), but the lowest concentration was still more potent than the generic cream at 0.1%.

After we developed the UVA-neutrophil assay for the anti-inflammatory efficacy of corticosteroids (7), we were interested in using the model to address the generic question. We included, within a series of different potency corticosteroids, two concentrations of desoximetasone (Topicort®, 0.05 and 0.25% emollient cream) and a generic brand (Taro, 0.05 and 0.25%). As in other published reports, we found a significant reduction in potency in the generic product.

MATERIALS AND METHODS

The UVA source, irradiation parameters and quantification of neutrophils are described in the accompanying paper (7). In this study there were some differences in methodology. Briefly, the Sky-hairless-1 (albino) mice were obtained from Charles River Laboratories (Wilmington, MA, USA) and there were 5 animals per treatment group.

To prevent undue discomfort to the mice, irradiation was confined to a 2 x 2 cm square of the dorsal trunk which was outlined with opaque tape. The remainder of the dorsal surface was treated with a broad spectrum (sun protection factor 15) sunscreen. Because exposure time was 200 min, mice were anesthetized with an intraperitoneal injection of 100 µl of a 1:9 dilution of γ-hydroxybutyric acid lactone (Sigma Chemical Co., St. Louis, MO).

In order to better approximate human use of corticosteroids, treatment schedule in this study was longer than that used in the development of the assay (7). Steroid treatment was once daily for 7 days. Irradiation was on the 8th day. The results of neutrophil quantification were analysed by a paired t-test at the 95% confidence level.

RESULTS

All steroid-treated animals had significantly less neutrophil infiltration than the UVA controls (Figs. 1 and 2). Additionally, the higher potency steroids reduced the neutrophil count to a significantly greater degree than those of lower potency (Fig. 1).

A comparison of the higher concentration (0.25%) generic desoximetasone to the brand name (Fig. 2) showed the latter to be significantly more potent in reducing the neutrophil count (p = 0.004). The difference between the two brands at 0.05% was not significant, but there was a trend for the name brand to be more potent than the generic. However, the lower concentration name brand steroid (0.05%) was marginally significantly more potent than the high concentration (0.25%) generic (p < 0.05). The name brand, at the two concentra-
this assay, hydrocortisone cream tested at 1% resulted in an intermediate count of 45.

The UVA-induced dermal neutrophil infiltration assay for corticosteroid potency has added to the evidence that generic brands can be less efficacious in suppressing inflammation than equal concentrations of name brand corticosteroids. The clinical implications with regard to the two brands tested in this study are identical to those expressed by others (4, 6, 8, 9). It is agreed that generic substitutions for name brand corticosteroids are not acceptable unless proof is provided for their equivalence in potency assays as well as in clinical applications.

REFERENCES