

Patch testing to detect corticosteroid allergy: is it adequate?

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Whilst patch testing with corticosteroids in ethanol is more sensitive than either petrolatum or the cream formulation, the frequency of false-negative reactions is not known. We have compared patch testing with corticosteroid at 1% in ethanol with intradermal (i.d.) tests using 1mg corticosteroid suspended in normal saline. Patch tests with tixocortol pivalate and budesonide detected all patients allergic to hydrocortisone and budesonide, respectively. For other corticosteroids, the use of ethanol as a vehicle resulted in both false-positive and false-negative reactions. In particular, patch tests with hydrocortisone-17-butyrate missed 30% of all positive reactions detected by i.d. testing. There may be a case for advising the avoidance of this steroid in all patients who are positive on patch testing to tixocortol pivalate and budesonide.

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Contact hypersensitivity to topical corticosteroids is well-recognized; in some centres, it is present in 2-5% of patients attending contact dermatitis clinics (1). The use of tixocortol pivalate (1% pet.) and budesonide (1% eth.) in the standard series detected 90% of cases of corticosteroid hypersensitivity (2). In this study, the addition of 3 other steroids (1% eth.), selected on the basis of local usage, detected 99% of all steroid-sensitive patients.

The ideal concentration and vehicle for detecting corticosteroid allergy has not been established.

For many corticosteroids, a 1% dilution in ethanol has been suggested as ideal (3-5). However, for budesonide, the use of petrolatum as vehicle (3, 6), and for hydrocortisone the use of tixocortol pivalate in petrolatum (7, 8), have been found to produce equivalent results. The use of the cream formulation may result in false-positive reactions due to excipient within the creams (3).

We have previously detected additional corticosteroid allergies in patients using intradermal (i.d.) tests (9, 10). The aim of this study was to assess whether using the most sensitive method of detecting corticosteroid allergy so far established (1% eth.) was equivalent to the results of i.d. testing.

Patients and Methods

Patients attending a contact dermatitis clinic were included if they had a positive patch test to one of 6 screening corticosteroids in our modified standard series. They were then patch tested to 17 corticosteroids available in the UK and had i.d. tests to a maximum of 8 corticosteroids. Patch tests were performed using Finn Chambers on Scanpor tape left on the skin of the back for 2 days. The patch tests were read at 2 and 4 days. Reactions were scored as recommended by the International Contact Dermatitis Research Group and were considered positive when an indurated erythematous (+) reaction or greater was present. I.d. tests were performed with 1 mg of pure corticosteroid suspended in 0.9% sterile saline.

Results

The results are summarized in Table 1. Patch tests with tixocortol pivalate and budesonide detected all patients i.d. test positive to hydrocortisone and budesonide, respectively. For the following steroids, i.d. tests produced additional positive reactions: hydrocortisone-17-butyrate (30% of allergic patients missed by patch testing), methylprednisolone, fluocortolone, halcinonide, clobetasol pro-

Table 1. Results of intradermal tests in 37 corticosteroid-allergic patients correlated with the results of patch tests. (discrepant results highlighted)

Intradermal tests	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37
hydrocortisone	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+
hydrocortisone-17-butyrate	0-	0-	0-	1-	0-	0-	0-	0-	0-	0-	0-	1-	0-	0-	1-	0-	0-	0-	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+
betamethasone valerate	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-
budesonide	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-
clobetasol propionate	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-
clobetasone butyrate	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-
alcometasone dipropionate	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-
beclomethasone dipropionate	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-
betamethasone dipropionate	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-
desoxymethasone	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-
diflucortolone valerate	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-
fluocinolone acetonide	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-
fluocinonide	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-
fluocortolone	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-
flurandrenolone	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-
halcinonide	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-
methylprednisolone	0-	0-	0-	1-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-
triamcinolone acetonide	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-	0-

Intradermal test: 0=negative; 1=positive.

Patch test: + = positive (for hydrocortisone patch test was with triamcinolone pivalate); - = negative; ? = positive but not reproducible; † = positive and reproducible.

pionate, flurandrenolone and triamcinolone acetonide. 6 reactions to screening corticosteroids on patch testing were not confirmed on i.d. testing and were negative on repeat patch testing. In 2 patients, a positive patch test to clobetasone butyrate was reproducible but negative on i.d. testing. A repeated open application test (ROAT), in 1 of these 2, was positive after 2 weeks.

Discussion

This study confirmed earlier studies that patch testing with tixocortol pivalate 1% pet. detects all patients with positive i.d. tests to hydrocortisone succinate (7, 11). This was shown to be both sensitive and specific (8). Similarly, patch tests with budesonide (1% pet. or eth.) detected all patients with positive i.d. reactions to budesonide. Patch testing for these 2 steroids detected all patients allergic to hydrocortisone and budesonide.

For the other steroids tested, i.d. tests produced additional positive reactions to hydrocortisone-17-butyrate, methyl prednisolone, fluocortolone, halcinonide, clobetasol propionate, flurandrenolone and triamcinolone acetonide. This finding suggests that, at present, hypersensitivity to corticosteroids may be missed by using the current optimum patch test method as the sole investigative tool.

It was notable that 30% of allergic reactions to hydrocortisone-17-butyrate were missed by patch testing. We have found similar results in an earlier study (10). 44% of patients allergic to tixocortol pivalate/hydrocortisone (12) and 72% allergic to budesonide (13) are patch test positive to hydrocortisone-17-butyrate. In such patients, it may be prudent to advise that hydrocortisone-17-butyrate is avoided, even when the patch test is negative, because of the high number of false-negative results. Based on these results, one might expect 17% of patients positive to tixocortol pivalate but negative to hydrocortisone-17-butyrate on patch testing to have a positive i.d. test. Given the number of false-negative reactions to other steroids, the choice of an alternative should be guided not only by the results of patch testing but also by what is known of corticosteroid cross-reaction patterns (12-14).

A number of positive patch test reactions were not confirmed on i.d. testing. When the patch tests were repeated, they were not reproducible in 6 out of 8 instances. We have assumed that these were irritant false-positive reactions caused by the ethanol. This emphasizes the importance of considering the relevance of any reaction and the use of a ROAT in certain instances. In the other 2 patients, both positive to clobetasone butyrate, the patch test results were reproducible and a ROAT was

positive in 1. This false-negative i.d. reaction may have been due to the use of corticosteroid as a suspension in saline. Corticosteroids have varying solubility in aqueous solution (15), and, for those that are water soluble, the use of saline for the i.d. test may be appropriate. The majority of corticosteroids giving additional positive reactions on i.d. testing were soluble in an aqueous:ethanol mixture in a previous study (15), while those without additional positive reactions were insoluble (including clobetasone butyrate). Unfortunately, for those corticosteroids that are poorly water soluble, alternative vehicles may be irritant when injected into the dermis (16). Using a suspension in saline may result in poor bioavailability and a false-negative reaction for those corticosteroids that are insoluble in water.

We conclude that patch tests with tixocortol pivalate and budesonide detect all patients allergic to hydrocortisone and budesonide, respectively. For other corticosteroids, the use of ethanol as a vehicle, while more sensitive than other methods currently available, may result in both false-positive and false-negative reactions. The search for a vehicle that ensures that patch tests are both sensitive and specific in the detection of corticosteroid contact allergy needs to continue.

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