

Detection of contact hypersensitivity to corticosteroids in allergic contact dermatitis patients who do not respond to topical corticosteroids

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The delayed hypersensitivity development against topical corticosteroids which are used in allergic contact dermatitis (ACD) treatment is an important clinical problem. In our study, 41 ACD patients who did not show any response to topical corticosteroid treatment were patch tested with corticosteroid series and the commercial preparations of corticosteroids and their vehicles. In corticosteroid series, there were budesonide, bethametasone-17-valerate, triamcinolone acetonide, tixocortol pivalate, alclomethasone-17-21-dipropionate, clobetasole-17-propionate, dexamethasone-21-phosphate disodium and hydrocortisone-17-butyrate. We detected positive reaction to corticosteroids in 9 of our cases (22%) (5 single and 4 multiple). The sensitivity was mostly produced by tixocortol pivalate (6 patients). This was followed by triamcinolone acetonide (2 patients) budesonide (2 patients), alclomethasone dipropionate (2 patients), dexamethasone 21 phosphate disodium (2 patients) and betamethasone-17-valerate (1 patient). As a result, it should not be forgotten that the corticosteroids used to treat ACD patients may cause ACD themselves. In ACD patients who did not respond to corticosteroid treatment, routinely applying patch test with corticosteroids should be helpful in directing the treatment.

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Topical steroids are the most important therapy used in allergic contact dermatitis (ACD). But contact sensitivity from steroids themselves is becoming increasingly reported in the past decade (1, 2). It should be suspected, especially, if there is no response to steroid therapy or worsening in the pre-existing lesions (3–37).

The aim of our study was to find out the frequency of hypersensitivity to corticosteroids among ACD patients who showed no response to corticosteroid therapy or worsening of the pre-existing lesions during corticosteroid therapy with patch testing.

Materials and Methods

Allergic contact dermatitis patients who had previously used various corticosteroid therapies with no response or worsening of the lesions were included in our study.

Our study group consisted of 41 patients, 17 males and 24 females; 33 patients had ACD and 8 had stasis ulcer with ACD.

The age, occupation, hobbies, the last date of menstruation for women patients, the signs, localization and duration of the disease and previous medications were learned.

Patients who had used topical steroids and oral antihistamines in the last week and systemic steroids in the last 3 weeks were excluded from the study.

European standard series (Trolab, Boots Healthcare International, Prague, Czech Republic) and corticosteroid standard series (Chemotechnique and Diagnostics CS 1000, Dormer Laboratories, Rexdale, Canada) were applied to the patients. Corticosteroid standard series included budesonide, betametasone-17-valerate, alclomethasone 17-21-dipropionate, triamcinolone acetonide, tixocortol pivalate, clobetasol-17-propionate, dexametasone-21-phosphate disodium and hydrocortisone-17-butyrate. The steroids that were suspected to exacerbate ACD during the therapy were applied in both commercial forms and as vehicles, without corticosteroids.

The patch test readings were conducted following International Contact Dermatitis Research Group guidelines after 48 hr and also after 4, 6 and 9 days for detection of possible late reactions.

Results

Our study was performed in 41 patients between 17 and 70 years (mean 33 ± 13 years). 24 of them were female and 17 were male. 32 of the patients had history of ACD and 8 of them had stasis dermatitis.

The location of ACD was on the hands in 24 patients, on the face in 2 patients, on the arms, face and hands in 5 patients, in the inguinal region in 1 patient and around stasis ulcer lesions on the leg in 8 patients.

In 32 patients, positive reaction was found to European standard patch test series. Positive reaction to 1 substance was found in 15 patients and more than 1 substance was found in 17 patients. 4 of the patients who had multiple positive reactions had stasis ulcers.

8 of the patients had positive reactions to nickel, 6 to potassium dichromate, 5 to cobalt chloride, 5 to formaldehyde, 5 to Peru balsam, 4 to thiuram mix, 4 to neomycine, 2 to mercapto mix, 2 to fragrance mix, 1 to paraphenylenediamine, PPD mix black rubber, wool alcohol, paraben mix and paratertier butyl phenol formaldehyde resin.

Positive reaction was found in 9 (22%) of the patients to corticosteroid series (Table 1). 5 had 1 and 4 had multiple positive reactions. One of the patients with positive reactions had stasis ulcer.

In addition to patch testing with the standard series, patch testing with commercial preparations and vehicles was done and positive

reactions were found to Prednol[®] cream (0.125% prednisolone) in 2 patients, Beklazon[®] cream (0.025% beclomethasone dipropionate) and its vehicle in 1 patient, Elocon[®] cream (0.1% mometasone furoate) and its vehicle in 1 patient.

Discussion

Allergic contact dermatitis to steroids is more common than it is thought because of their widespread use (14).

Contact sensitivity to corticosteroids is seen clinically as a dermatosis unresponsive to steroids or worsening of pre-existing dermatosis (4, 5, 7, 13–17, 19, 20). Although topical corticosteroid therapy reduces the number of Langerhans' cells and their immune functions, it cannot prevent the sensitivity to itself and can cause exacerbation of the dermatosis in sensitive patients (10, 12, 23).

The incidence of sensitivity to corticosteroids varies between 0.2 and 5% (3, 6–8, 12, 24, 22). In a European Environmental Contact Dermatitis Research Group study, corticosteroid allergy was found to be 2.6% in Europe (33). In Turkey, corticosteroid sensitivity incidence was 5% (26). The discrepancy between the incidences of corticosteroid sensitivities may be due to geographical conditions, the type of steroids that the dermatologists tend to use, the frequency and amount of steroid usage, the type of steroids and their vehicles chosen for patch testing, test concentrations, testing methods other than patch testing like intradermal testing and the patient group chosen for the study (7–12).

In 2 earlier studies, it was found that the severity of responses, which were positive in the first assessment, increased, and the number of positive reactions were maximum in the second day

Table 1. Positive reactions to European corticosteroid patch testing series

Diagnosis	Age	Sex	Corticosteroids	48 hr	4 days	6 days	9 days
ACD	21	Female	Tixocortol pivalate	++	+	–	–
ACD	25	Female	Triamcinolone acetonide	++	+	+	–
			Tixocortol pivalate	–	+	+	–
ACD	26	Male	Alclometasone dipropionate	+	+	–	–
ACD	22	Female	Tixocortol pivalate	+	–	–	–
ACD	20	Male	Budesonide	++	+	+	–
			Alclometasone dipropionate	–	+	+	–
			Dexamethasone-21-phosphate disodium	+	+	–	–
ACD	30	Female	Tixocortol pivalate	++	+	–	–
ACD	26	Male	Triamcinolone acetonide	+	+	–	–
			Tixocortol pivalate	++	+	+	+
			Dexamethasone-21-phosphate-disodium	+	+	–	–
ACD	32	Female	Tixocortol pivalate	+	+	–	–
ACD + stasis ulcer	37	Male	Budesonide	++	++	+	+
			Betamethasone-17-valerate	+	+	–	–

ACD, allergic contact dermatitis.

(11, 14). We also found positive reactions in the first assessment and more positive reactions were found to 2 more steroids in the fourth day. We did not detect an increase in the severity of the reaction. This is in contrast to the findings of Isaksson et al. who state that without late reading up to 30% of contact allergy to corticosteroids is missed but in agreement with Steven et al. (34, 35).

The probability of ACD to steroids is reported to be more common in patients with stasis dermatitis and leg ulcers; moreover, in some studies steroid sensitivity was reported to be more common in those patients than in patients with hand eczema (19, 27, 36). We included 24 patients with hand eczema in our study and found sensitivity to corticosteroids in 6 of them, and we found sensitivity to corticosteroids in 25% of hand eczema patients and 12% of patients with stasis ulcers.

Dooms-Goossens (19) reported that there was more sensitivity to corticosteroids in patients with chronic eczema and multiple topical drug sensitivity. In another study, Wilkinson et al. reported that eczema duration was not a determining prognostic factor for development of corticosteroid sensitivity. In our study, the duration of dermatitis in patients with corticosteroid sensitivity was 1 year or more except 1 patient. There was sensitivity to drugs other than steroids especially in 5 patients of whom 3 had stasis ulcers.

It is reported that because steroid standard series did not include all corticosteroids that cause sensitivity, patch testing with suspected corticosteroids should be done. Also patch testing with vehicles of commercial preparations should be done, because they can also be responsible for unresponsiveness to treatment (12, 16, 30).

Because we found positive reactions to steroid preparations as well as their vehicles in 4 patients, we thought that the reactions were to the vehicles of the steroids.

In our study, we found corticosteroid sensitivity only in 9 patients (22%) who were suspected to have steroid allergy. While a corticosteroid can cause ACD in a commercial preparation with vehicles that increase penetration, in a neutral vehicle it can cause negative patch test results. While application to damaged skin where penetration is higher can cause ACD, patch tests applied to normal skin can cause negative results. Use of other vehicles than petrolatum increase penetration and the probability of positive reactions (3, 13, 14, 23, 24, 25, 29, 31).

In conclusion, patch testing with steroids as a rule in ACD patients who do not respond to corticosteroid therapy will help to direct therapy. Standard series with appropriate vehicles and concentrations must be used to detect corticosteroid

allergy. Investigation of the effects of penetration and anti-inflammatory properties of corticosteroids on patch tests done with corticosteroids will help to detect sensitivity to corticosteroids.

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