

Contact allergy to prednicarbate: frequency of positive reactions in consecutively-patch-tested patients

LUCA STINGENI AND PAOLO LISI

Allergologic and Environmental Dermatology Unit, Department of Medical and Surgical Specialities,
University of Perugia, Policlinico Monteluce, I-06100 Perugia, Italy

Key words: prednicarbate; corticosteroids; contact allergy; frequency; patch test; cross-sensitivity; medicaments.
© Munksgaard, 1999.

Class D corticosteroids (CSs) have a long-chain ester at C₁₇ and/or C₂₁, with or without a C₁₆-methyl substitution (1). Esterification of polar groups increases lipophilicity and probably percutaneous penetration (2), which might explain the sensitizing effect of hydrocortisone-17-butyrate (3). Prednicarbate (P), a class D non-halogenated high-potency CS, is a prednisolone derivative esterified in the 17 and 21 positions by an ethylcarbonate and a propionate group, respectively (Fig. 1). After cutaneous permeation, P is hydrolyzed by skin esterases to prednisolone-17-ethylcarbonate and prednisone (4), two class A compounds. Topical P was recently also marketed in Italy.

Patients and Methods

From February 1998 to July 1998, 325 consecutive patients with contact dermatitis (113 male, 212 female, mean age 38.2 years, range 5–85 years) were patch tested with the GIRDCA standard series and P (1% eth. and pet.) on the upper back, using Van der Bend square chambers and reading according to ICDRG criteria at day (D) 2, 4 and, when possible, 6. When P was positive, the CS series in Table 1 was applied.

Results

Only 2 subjects (0.62%) showed positive reactions to P, in both eth. and pet. (Table 1). The 1st, a 49-year-old non-atopic woman, had had recurrent allergic contact dermatitis of the face, caused by cosmetics and treated with topical betamethasone-17-valerate or mometasone furoate. Multiple positive patch test reactions to CSs were seen (Table 1): 3 due to class B compounds (budesonide, triamcinolone acetonide, fluocinolone acetonide) and 2 to class D (betamethasone-17-valerate, hydrocorti-

sone-17-butyrate). Therefore, the sensitivity to P was a cross-reaction to betamethasone-17-valerate and probably to mometasone, another class D CS.

The 2nd subject, a 29-year-old non-atopic woman, was investigated for acute contact dermatitis of the lower limbs, following repeated occlusion with topical budesonide for a granulomatous tick-bite reaction. She had a past history of dermatitis from topical drugs (Table 1). Patch testing with the CS series showed positive reactions to budesonide (class B CS), hydrocortisone-17-butyrate and fluocortolone caproate (class D CSs).

Discussion

There was a low frequency of positive reactions to P (0.62%) despite the selection of patients, all of whom had had contact dermatitis for varying periods and had used topical CSs of various strengths, though not P. A low sensitizing capacity was also already shown by

Table 1. Patch test results in 2 patients sensitized to prednicarbate

Allergens	Patient no. 1		Patient no. 2	
	D2	D4	D2	D4
prednicarbate ^{a)}	++	++	++	++
prednicarbate ^{b)}	++	++	++	++
<i>Corticosteroid series¹</i>				
hydrocortisone-21-acetate (A)	—	—	—	—
methylprednisolone (A)	—	—	—	—
fludrocortisone (A)	—	—	—	—
fluorometholone (A)	—	—	—	—
budesonide (B)	+++	+++	+++	+++
triamcinolone acetonide (B)	++	++	—	—
fluocinolone (B)	++	++	—	—
desoxymethasone (C)	—	—	—	—
fluocortolone (C)	—	—	—	—
hydrocortisone-17-butyrate (D)	+	+	—	++
fluocortolone caproate (D)	—	—	++	++
betamethasone-17-valerate (D)	—	++	—	—
difluocortolone pivalate (D)	—	—	—	—
<i>GIRDCA standard series</i>				
balsam of Peru (25% pet.)	++	++	—	—
ethylenediamine dichloride (1% pet.)	—	—	+++	+++
fragrance mix (8% pet.)	++	++	++	++
neomycin sulfate (20% pet.)	—	—	++	++
p-phenylenediamine (1% pet.)	++	++	—	—
wool p wax alcohols (30% pet.)	++	++	—	—

^{a)}1% eth.; ^{b)}1% pet.

In brackets, the CS classes (1).

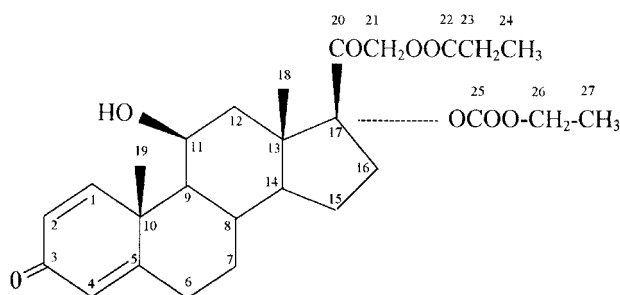


Fig. 1. Chemical structure of prednicarbate.

Dooms-Goossens et al. (5) who, in 1991, compared contact allergy to CSs in 2 centres, Leuven (Belgium) and Amsterdam (The Netherlands). The frequency of reactions to CSs differed between the 2 centres, but not that to P (0.65% and 0.37%, respectively), probably because it was not yet commercially available. Since then, only 3 cases of allergic contact dermatitis have been described: the 1st (6) in a German woman with recurrent leg ulcers, also sensitized to hydrocortisone-17-butyrate and budesonide; the 2nd (7) in a Spaniard with multiple positive patch test reactions to CSs (hydrocortisone-17-butyrate, betamethasone valerate and dipropionate, budesonide, triamcinolone acetonide, tixocortol pivalate); the 3rd (8) in a Spaniard with pruritus and burning sensation of the penis and scrotum, allergic to hydrocortisone (used in the past), hydrocortisone-17-butyrate, and tixocortol pivalate.

Although not always explicitly reported, sensitivity to P seems to be induced by CSs of class D (in particular, hydrocortisone-17-butyrate and betamethasone-17-valerate) and/or B (above all, budesonide and triamcinolone acetonide). This hypothesis is supported by 19 positive reactions to P 1% eth. observed by Lepoittevin et al. (9) in 105 patients sensitized to CSs, and by a statistically significant correlation found between positive tests to budesonide and hydrocortisone-17-butyrate (3). The class A CSs, in which the P metabolites are included, are less relevant.

Acknowledgement

We thank Hoechst AG of Frankfurt, Germany, for providing the prednicarbate.

Patch testing with nickel sulfate versus nickel chloride

LIISA RÄSÄNEN, ULLA MATTILA¹ AND KIRSTI KALIMO¹

Department of Dermatology, University Hospital of Kuopio, P.O. Box 1777, FIN 70211 Kuopio, Finland,

¹Department of Dermatology, University Central Hospital of Turku, Turku, Finland

Key words: nickel sulfate; nickel chloride; patch test; lymphocyte proliferation test; contact allergy. © Munksgaard, 1999.

5% nickel sulfate in pet. may give false-negative results (1–3); hence, testing with nickel chloride (4–6), occlusion or detergent pre-treatment of the patch test sites (7) and using different vehicles or penetration enhancers (8–10). Permeation of nickel through the skin takes place faster from chloride than from sulfate (11).

Subjects and Methods

Study populations

The study was carried out at the Departments of Dermatology, University Hospitals of Kuopio and Turku, Finland. The data base on patch-tested patients in 1996 was utilized, and those exhibiting an allergic or irritant reaction to NiSO₄, NiCl₂ or both, were selected. Altogether, 1281 subjects were patch tested. The history with regard to nickel was obtained from files or via enquiry from patients with discordant patch test reactions to

nickel compounds. The patients were asked if they had noticed any skin symptoms from various nickel-containing metal items worn or otherwise in contact with, a positive history for nickel thus being defined as dermatitis from nickel contact.

Patch tests

Patch tests were performed with the standard series (NiSO₄ 5% pet. included) and NiCl₂ 2.5% pet. Some of the patients were also tested with NiCl₂ 5% and 1% pet. The patch tests were applied with Finn Chambers® on Scanpor®. The occlusion time was 2 days and the results were also read on D 4.

Lymphocyte proliferation test

Peripheral blood lymphocytes isolated by Ficoll-Isoopaque centrifugation were cultured in the presence of NiSO₄, NiCl₂ or a medium only. The cells were cultured

References

1. Coopman S, Dooms-Goossens A. Cross-reactions in topical corticosteroid contact dermatitis. *Contact Dermatitis* 1988; 19: 145–146.
2. Dunkel F G, Elsner P, Burg G. Contact allergies to topical corticosteroids: 10 cases of contact dermatitis. *Contact Dermatitis* 1991; 25: 97–103.
3. Dooms-Goossens A, Andersen K E, Brandaõ F M, Bruynzeel D, Burrows D, Camarasa J, Ducombs G, Frosch P, Hannuksela M, Lachapelle J M, Lahti A, Menné T, Wahlberg J E, Wilkinson J D. Corticosteroid contact allergy: an EEC DRG multicentre study. *Contact Dermatitis* 1996; 35: 40–44.
4. Poertner M, Moellmann H, Rohdewald P. Glucocorticoid receptors in human synovial tissue and relative receptor affinities of glucocorticoid-21-esters. *Pharmaceut Res* 1988; 5: 623–627.
5. Dooms-Goossens A, Meinardi M M H M, Bos J D, Degreëf H. Contact allergy to corticosteroids: the results of a two-centre study. *Br J Dermatol* 1994; 130: 42–47.
6. Dunkel F G, Elsner P, Burg G. Allergic contact dermatitis from prednicarbate. *Contact Dermatitis* 1991; 24: 59–60.
7. Villas Martínez F, Navarro Echeverría J A, Joral Badás A, Garmendia Goitia F J. Prednicarbate contact allergy. *Contact Dermatitis* 1997; 37: 299–300.
8. Miranda-Romero A, Sánchez-Sambucety P, Bajo C, Martinez M, Garcia-Muñoz M. Genital oedema from contact allergy to prednicarbate. *Contact Dermatitis* 1998; 38: 228–229.
9. Lepoittevin J-P, Drieghe J, Dooms-Goossens A. Studies in patients with corticosteroid contact allergy: understanding cross-reactivity among different steroids. *Arch Dermatol* 1995; 131: 31–37.