Contact Hypersensitivity to European Baseline Series and Corticosteroid Series Haptens in a Population of Adult Patients with Contact Eczema

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ABSTRACT Contact eczema (CE) is one of the most common skin diseases and is regarded as a reaction pattern. However, the skin can react in the same way to different stimuli, some of which may act together. The golden standard in the diagnosis of allergic contact dermatitis (ACD) is the patch test. Contact allergy to topical corticosteroids is known to be gradually rising, and this represents a significant problem in the treatment of contact eczema.

The aim of this study was to evaluate the prevalence of contact allergy to European Baseline Series and Corticosteroid Series haptens in a population of patients with CE.

A group of 126 patients with the clinical diagnosis of contact eczema were patch tested with 28 European Baseline Series allergens and 8 corticosteroid allergens in different concentrations and in different media: 80 (64.5%) women and 46 (36.5%) men, mean age 50.4 years. The average duration of CE was 6.9 years.

In total, 65 patients (51.6%) demonstrated an allergic reaction to at least one European Baseline Series allergen, and 22 patients (17.4%) to at least one corticosteroid. The most common allergens giving positive results were nickel sulfate (26.2%), cobalt chloride (15.1%), budesonide (14.3%), potassium dichromate (13.5%), and myroxylon pereirae resin (MPR) (11.9%). According our data, the European Baseline Series tests allow the cause of ACD to be identified in over 50% of cases.

KEY WORDS: contact hypersensitivity, European baseline series haptens, contact eczema

INTRODUCTION

Allergic contact dermatitis (ACD) is the consequence of exposure to a hapten in a contact-sensitized individual. Gell and Coombs classify ACD as a classic example of cell-mediated immune response resulting from type IV hypersensitivity. ACD requires the activation of antigen-specific acquired immunity, leading to the development of effector T cells which mediate skin inflammation (1). Contact dermatitis is one of the most common skin diseases, and has a considerable socio-economic impact. However, although

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the exact prevalence of contact allergy is unknown, allergic contact dermatitis may affect up to 55% of the adult population (2). There are also differences in the frequency of contact allergy to specific substances among citizens of different countries (3).

Contact allergy to corticosteroids is becoming increasingly recognized worldwide as a problem of considerable clinical and therapeutic importance, and was first observed soon after their introduction in the early 1950s. Burckhardt reported the first case of allergic contact dermatitis to hydrocortisone in 1959, and in that same year, Kooij reported ACD to both hydrocortisone and neomycin (4,5). ACD to steroids should be suspected if dermatitis worsens or does not improve following their use (6). The incidence of corticosteroid allergy is known to vary from 0.5% to 10.7%, depending on the center (7,8). This paper presents our clinical experience with patch testing using the European Baseline Series and corticosteroid haptens in a specific population of patients with contact eczema.

PATIENTS AND METHODS

One hundred and twenty-six patients with contact eczema under the care of the Department of Dermatology and Venereology, Medical University of Lodz were examined. The diagnosis of contact dermatitis was established on the basis of clinical signs, medical history, and histopathological examination where necessary. Eighty patients were women and 46 were men (age range: 19-82 years, mean age 50.4). Before applying the patch tests, a detailed interview was performed concerning the previous course of the disease and the treatment. The disease duration ranged from 2 months to 42 years, with a mean duration of 6.9 years.

The interview focused on the use of applicable topical corticosteroids. The duration of topical steroid use (on and off) ranged from 0 to 20 years (mean 4.2 years). In total, 74 (58.7%) patients were using local therapy ointments containing corticosteroids from group A, 30 (23.8%) from group B, 12 (9.5%) from group C, 89 (70.6%) from group D1, and 40 (31.7%) from group D. Many patients used ointments containing different groups of corticosteroids. Five patients had never used topical corticosteroids; they were treated with moisturizing ointments and pimecrolimus. No patients were taking systemic corticosteroids, immunosuppressive drugs, or antihistamines during the examination.

Patch testing was only performed on patients in whom any treatment with antihistamines had been stopped in the previous week or immunosuppressive drug treatment in the previous two weeks. Although skin lesions were sometimes present during patch testing, their severity and location did not prevent the tests from being performed. In total, 111 (88.1%) patients experienced skin lesions on the hands, 25 (29.8%) on the feet, 52 (41.3%) on the lower legs, 34 (27.0%) on the trunk, and 40 (31.7%) on the face. Only moisturizing ointments were permitted during patch testing. Patients were patch tested with 28 European Baseline Series allergens and 8 corticosteroid allergens at a range of concentrations and in various media (Table 1, Table 3). Chemotechnique Diagnostics allergens were used in this study.

We used 8 corticosteroid allergens in petrolatum base: budesonide (0.1% and 0.01%), betamethasone-17-valerate (0.1%), triamcinolone acetonide (1%), alclomethasone-17,21-diproponate (1%), clobetasol-17-propionate (1%), dexamethasone-21-phosphate disodium salt (1%), tixocortol-21-pivalate (0.1%), and hydrocortisone-17-butyrate (1% in alcohol and in petrolatum). Patch tests were read in all patients after 2, 3, 4, 5, and 7 days since applications.

RESULTS

Allergic reactions to at least one European Baseline Series allergen were observed in 65 patients (51.6%). The most common allergens giving positive results were nickel sulfate (26.2%), cobalt chloride (15.1%), potassium dichromate (13.5%), 0.01% budesonide (12.7%), 0.1% budesonide (11.9%), and myroxylon pereirae resin (MPR) (11.9%) (Table 1).

The most common forms of hypersensitivity observed among female patients were to nickel sulfate (35%), cobalt chloride (20%), potassium dichromate (13.7%), 0.01% budesonide (13.7%), and MPR (8.7%). In male patients, the hypersensitivites most commonly observed were to MPR (17.4%), potassium dichromate (13%), 0.01% nickel sulfate (10.9%), and budesonide (10.9%).

In 33 patients under the age of 40, nickel sulfate (33.3%), cobalt chloride (18.2%), potassium dichromate and MPR (12.1% each) were the most common contact allergen. In 93 patients over the age of 40, allergy to nickel sulfate was observed in 23.7% of patients, while allergies to cobalt chloride, potassium dichromate, and 0.01% budesonide were each observed in 14%.

In patients with a duration of contact eczema of less than 5 years (73 patients), the most common sensitizing allergens were nickel sulfate (23.3%), cobalt chloride (17.8%), potassium dichromate (12.3%), and 0.01% budesonide (11,0%). In those suffering over 5 years (53 patients), the most common were nickel

Table 1. Prevalence of contact allergy to European Baseline Series haptens

Allergen	Positive reactions													
	Female (n=80)		Male (n=46)		Total (n=126)		Age <40 (n=33)		Age >40 (n=93)		Duration of CE (years)			
											<5 (n=73)		>15 (n=53)	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Potassium dichromate 0.5%	11	13.7	6	13.0	17	13.5	4	12.1	13	14.0	9	12.3	8	15.1
Phenylenediamine 1%	3	3.7	2	4.3	5	3.9	3	9.1	2	2.1	1	1.4	4	7.5
Thiuram mix 1%	1	1.2	1	2.2	2	1.6	0	0.0	2	2.1	1	1.4	1	1.9
Neomycin sulfate 20%	2	2.5	0	0.0	2	1.6	0	0.0	2	2.1	1	1.4	1	1.9
Cobalt chloride 1%	16	20.0	3	6.5	19	15.1	6	18.2	13	14.0	13	17.8	6	11.3
Benzocaine 5%	1	1.2	2	4.3	3	2.4	0	0.0	3	3.2	1	1.4	2	3.8
Nickel sulfate 5%	28	35.0	5	10.9	33	26.2	11	33.3	22	23.7	17	23.3	16	30.2
Clioquinol 5%	2	2.5	0	0.0	2	1.6	1	3.0	1	1.1	0	0.0	2	3.8
Colophonium 20%	1	1.2	2	4.3	3	2.4	1	3.0	2	2.1	1	1.4	2	3.8
Paraben mix 16%	3	3.7	1	2.2	4	3.2	0	0.0	4	4.3	1	1.4	3	5.7
P-Phenylenediamine 0.1%	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Lanolin alcohol 30%	1	1.2	0	0.0	1	0.8	0	0.0	1	1.1	0	0.0	1	1.9
Mercapto mix 2%	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Epoxy resin 1%	0	0.0	1	2.2	1	0.8	0	0.0	1	1.1	1	1.4	0	0.0
Myroxylon pereirae resin 25%	7	8.7	8	17.4	15	11.9	4	12.1	11	11.8	6	8.2	9	17.0
Para tertiary butylphenol formaldehyde resin 1%	1	1.2	1	2.2	2	1.6	0	0.0	2	2.1	1	1.4	1	1.9
2-Mercaptobenzothiazole 2%	0	0.0	1	2.2	1	0.8	0	0.0	1	1.1	0	0.0	1	1.9
Formaldehyde 1%	2	2.5	0	0.0	2	1.6	1	3.0	1	1.1	1	1.4	1	1.9
Fragrance mix I 8%	4	5.0	3	6.5	7	5.5	3	9.1	4	4.3	2	2.7	5	9.4
Sesquiterpene lactone mix 0.1%	0	0.0	3	6.5	3	2.4	0	0.0	3	3.2	1	1.4	2	3.8
Quaternium-15 1%	3	3.7	0	0.0	3	2.4	1	3.0	2	2.1	2	2.7	1	1.9
2-Methoxy-6-n-pentyl-4-benzoquinone 0.01%	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Methylisothiazolinon 0.01%	0	0.0	1	2.2	1	0.8	0	0.0	1	1.1	1	1.4	0	0.0
Budesonide 0.01%	11	13.7	5	10.9	16	12.7	3	9.1	13	14.0	8	11.0	8	15.1
Tixocortol-21-pivalate 0.1%	3	3.7	3	6.5	6	4.8	2	6.1	4	4.3	3	4.1	3	5.7
Methylodibromoglutaronitrile 0.5%	4	5.0	3	6.5	7	5.5	1	3.0	6	6.4	1	1.4	6	11.3
Fragrance mix II 14%	2	2.5	1	2.2	3	2.4	1	3.0	2	2.1	0	0.0	3	5.7
Lyral 5%	1	1.2	0	0.0	1	0.8	0	0.0	1	1.1	0	0.0	1	1.9

sulfate (30.2%), potassium dichromate and 0.01% budesonide (15.1% each), and cobalt chloride and methylodibromoglutaronitrile (11.3% each).

In our study, 22 patients out of 126 (17.4%) had an allergic reaction to at least one corticosteroid. The corticosteroid haptens giving most common positive results were 0.01% budesonide (12.7%), 0.1% budesonide (11.9%), and betamethasone and clobetasol (9.5% each) (Table 3). In female patients, the most commonly-observed reactions were to 0.01% budesonide (13.7%), 0.1% budesonide (9.0%), and betamethasone (7.0%), while in men 0.1% budesonide and clobetasol (13.0% each) and 0.01% budesonide and betamethasone (10.9% each) were the most common.

Hypersensitivity to a single corticosteroid was observed in 8 patients, to two corticosteroids in 2 patients, to three in 2 patients, to four in 2 patients, to six in 4 patients, to seven in 3 patients, and to eight in 1 patient. Sixteen (72.7%) patients with hypersensitivity to corticosteroids were also sensitized to non-steroidal haptens included in the European Baseline Series. The corticosteroids included in European Baseline Series (budesonide 0.01% and tixocortol-21-pivalate) revealed 19 (86.4%) cases of steroid allergy. Budesonide allergy was observed in 18 patients: 13 cases demonstrated a positive result for budesonide at both concentrations (0.1% and 0.01%), 3 cases at 0.01% and 2 cases at 0.1%. Allergy to hydrocortisone was observed in 12 patients: 7 cases with a positive result with hydrocortisone in petrolatum and alcohol,

Table 2. Characteristics of patients with contact allergy to corticosteroids

Sex	Age	Disease duration (years)	Lesion location	Duration of using steroids topically (years)	Applied substances contain steroids from groups	Positive tests
F	39	5	Hands, trunk	3	A	Chrome, cobalt, tixocortol
F	53	1	Hands, trunk, lower limbs	1	A, D1	Myroxylon pereirae resin, tixocortol
F	34	5	Hands	3	D1	Nickel, budesonide 0.01%
F	82	40	Lower legs	15	A, D1	Benzocaine, nickel, clioquinol, paraben mix, budesonide (0.01% and 0.1%)
F	54	8	Hands, feet, lower limbs	5	A, D1, D2	Nickel, budesonide (0.01%), tixocortol, hydrocortisone (1% alc.)
F	48	6	Hands, face	5	B, D1	Myroxylon pereirae resin, budesonide (0.01% and 0.1%)
F	37	1	Hands, face	1	A, D1	Cobalt, nickel, colophonium, myroxylon pereirae resin, budesonide (0.01% and 0.1%)
F	72	1	Hands, face	1	A, C, D1	Budesonide (0.01%), dexamethasone, hydrocortysone (1% alc.)
F	48	3	Hands, trunk	2	A, B, D1, D2	Chrome, nickel, myroxylon pereirae resin, budesonide (0.01% and 0.1%), betamethasone, clobetasol, hydrocortysone (1% waz.)
F	49	7	Hands, lower limbs	6	A, D1, D2	Cobalt, nickel, lanolin, budesonide (0.01% and 0.1%), methylodibromoglutaronitrile, betamethasone, triamcinolone, clobetasol, dexamethasone, hydrocortisone (1% alc. and petr.)
F	65	0.5	Hands, feet, trunk, face	0.5	A, B, D1, D2	Budesonide (0.01% and 0.1%), alclomethasone, betamethasone, triamcinolone, clobetasol, dexamethasone, hydrocortisone (1% petr.)
F	23	0.3	Hands, face, lower limbs	0.3	D1	Cobalt, nickel, betamethasone
F	54	5	Hands	1	A, D1	Nickiel, budesonide (0.1%), betamethasone, triamcinolone, clobetasol, dexamethasone, hydrocortisone (1% alc. and petr.)
F	40	15	Hands, feet, lower limbs	1	D1, D2	Budesonide (0.01% and 0.1%), betamethasone, triamcinolone, clobetasol, dexamethasone, hydrocortisone (1% alc. and petr.)
F	74	30	Hands, feet, lower limbs	20	A, B, C, D1, D2	Chrome, neomycin, cobalt, nickel, methylodibromoglutaronitrile, budesonide (0.01% and 0.1%), betamethasone, triamcinolone, clobetasol, dexamethasone, hydrocortisone (1% alc. and petr.)
M	68	42	Hands, lower limbs	20	A, B, D1	Myroxylon pereirae resin, colophonium, benzothiazole, fragrance mix I, budesonide (0.01% and 0.1%), tixocortol, alclomethasone, betamethasone, triamcinolone, clobetasol, dexamethasone, hydrocortisone (1% alc. and petr.)
M	82	15	Lower limbs	10	A, B, D1	Chrome,nickiel, myroxylon pereirae resin, budesonide (0.01% and 0.1%)
M	52	3	Hands, trunk, face	3	A, C, D1, D2	Chrome, cobalt, benzocaine, nickel, budesonide (0.01% and 0.1%), betamethasone, clobetasol.
M	55	3	Hands	1.5	A, D1	Budesonide (0.01% and 0.1%), betamethasone, triamcinolone, clobetasol, dexamethasone, hydrocortisone (1% alc. and petr.)
M	47	18	Hands, lower limbs	6	A, D1, D2	Benzocaine, colphonium, paraben mix, myroxylon pereirae resin, tixocortol, budesonide (0.1%), betamethasone, clobetasole
M	62	7	Hands	6	A, D1	Clobetasole, hydrocortisone (1% alc.)
M	29	2	Hands	1	A, D1	Budesonide (0.01% and 0.1%), tixocortol, betamethasone, triamcinolone, clobetasol, dexamethasone, hydrocortisone (1% alc. and petr.)

3 cases with only hydrocortisone in petrolatum, and 2 cases with hydrocortisone in alcohol.

Various sensitivities were found according to steroid group. Sensitivity to group B occurred in 14.3%, to group D1 in 11.1%, to group D2 in 10.3%, to group C in 7.9%, and to group A in 4% (Table 4). In the group of patients with hypersensitivity to steroids, the most frequently obtained cross-reactions were those between groups B and D (59.1%), B and D1 (50.0%), B and D2 (50.0%), and D1 and D2 (45.4%). The prevalence of allergy to the group of steroids according to topical steroid used is shown in Table 5.

DISCUSSION

In almost all developed countries, nickel is currently the most common contact allergen. While this phenomenon was only noticed in the late 90s in Poland, it has been known for many years in Western Europe (9). Contact allergy to nickel affects 17% of adults (10). Nickel allergy is more common among women than men, affecting an estimated 20% of the female and 6% of the male populations of Western Europe (11), and significantly higher among individuals with a positive history of pierced ears and jewelry rash (12,13). In 2002, Jensen *et al*. found nickel allergy to be present in 3.9% of 305 Danish schoolgirls aged 10-14 years and in 17.1% of 275 high-school girls aged 17-22 years, in whom the respective frequencies of ear piercing were 68.9% and 86.2% (13). This can be explained by the introduction of the Danish Nickel Regulation that reduced the allowable concentration of nickel in products authorized for sale (12). In 1994, the European Union introduced the Nickel Directive (13), which limited the nickel release threshold from alloys and nickel-plated objects which have prolonged contact with the skin. These migration limits are 0.2 μg/cm^2 per week for metal parts which are inserted into pierced ears and other pierced parts of the human body, and 0.5 μg/cm^2 per week for other products which have direct and prolonged contact with the skin (13). In the present study, 26.2% patients with CD, 35% of women and 10.9% of men, were found to be sensitized to nickel. The frequency of contact allergy to nickel is higher in younger people. Piaserico *et al*. found the frequency of nickel allergy to be 6.9% among the elderly and 24.2% among adults (14), while our present findings indicate the prevalence to be 33.3% among patients below 40 years of age and 23.7% for those aged over 40 years.

Our findings also indicate that cobalt allergy occurred in 15.1% cases: 20% of women and 6.5% of men. Cobalt allergy may affect up to 29.8% of patients with eczema (16). In 2008, Balato *et al*. demonstrated a cobalt prevalence of 7.7% in older patients (15). Isolated allergy to this metal is rare. Sensitization to cobalt usually coexists with allergy to chromium in men and to nickel in women (17). In the present study, 93.7% of women who demonstrated hypersensitivity to cobalt also were sensitized to nickel, while 100%

Table 3. Prevalence of contact allergy to corticosteroids haptens

Allergen	Group	Positive reactions													
		Women (n=80)		Men (n=46)		Total (n=126)		Age <40 (n=33)		Age >40 (n=93)		Duration of CE (years)			
												<5 (n=73)		>5 (n=53)	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Budesonide 0.1%	B	9	11.2	6	13.0	15	11.9	2	6.1	13	14.0	7	9.6	8	15.1
Betamethasone-17-valerate 0.1%	D1	7	8.7	5	10.9	12	9.5	2	6.1	10	10.7	7	9.6	5	9.4
Triamcinolone acetonide 1%	B	5	6.2	3	6.5	8	6.3	1	3.0	7	7.5	4	5.5	4	7.5
Alclomethasone-17,21-dipropionate 1%	D1	1	1.2	1	2.2	2	1.6	0	0.0	2	2.1	1	1.4	1	1.9
Clobetasol-17-propionate 1%	D1	6	7.5	6	13.0	12	9.5	1	3.0	11	11.8	6	8.2	6	11.3
Dexamethasone-21-phosphate disodium salt 1%	C	6	7.5	3	6.5	9	7.1	1	3.0	8	8.6	5	6.8	4	7.5
Hydrocortisone-17-butyrate 1% alk	D2	6	7.5	4	8.7	10	7.9	1	3.0	9	9.7	4	5.5	6	11.3
Hydrocortisone 1%	D2	6	7.5	3	6.5	9	7.1	1	3.0	8	8.6	5	6.8	4	7.5
Budesonide 0,01%	B	11	13.7	5	10.9	16	12.7	3	9.1	13	14.0	3	9.1	13	14.0
Tixocortol-21-pivalate 0.1%	A	3	3.7	3	6.5	6	4.8	2	6.1	4	4.3	2	6.1	4	4.3

*CE: contact eczema

Table 4. Prevalence of contact allergy to corticosteroids by group

Steroid group	Positive reactions													
	Women (n=80)		Men (n=46)		Total (n=126)		Age <40 (n=33)		Age >40 (n=93)		Duration of CE (years)			
											<5 (n=73)		>5 (n=53)	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
A	3	3.7	2	4.3	5	4.0	1	3.0	4	4.3	1	1.4	4	7.5
B	12	15.0	6	13.0	18	14.3	3	9.1	15	16.1	7	9.6	11	20.1
C	7	8.7	3	6.5	10	7.9	1	3.0	9	9.7	5	6.8	5	9.4
D1	8	10.0	6	13.0	14	11.1	2	6.1	12	12.9	7	9.6	7	13.2
D2	8	10.0	5	10.9	13	10.3	3	9.1	10	10.7	7	9.6	6	11.3

*CE: contact eczema

of the men allergic to cobalt were also sensitized to chrome.

Chrome is a common occupational allergen. Contact allergy to chrome is more frequent in men and older people (9). Common occupational sources are cement, chrome-tanned leather, bleaching agents, paints, and printing solutions. In patients with eczema, the frequency of hypersensitivity to chrome ranges from 5.0% to 20.6% (16,18). Our results showed that allergy to chrome occurred in 13.5% cases (13.7% of female and 13% of male patients). Its prevalence was 12.1% in patients aged below 40 years of age and 14% in those aged over 40 years.

Myroxylon pereirae resin is a natural substance used in the local treatment of burns, ulcers, and wounds. Its extracts and distillates are very often used as fragrant additives to cosmetics and can be an allergy marker to perfumes. In a study conducted by Avalos-Peralta *et al*. the prevalence of allergy to MPR was 5.79%, and was slightly higher in men (7.32%) than in women (4.91%) (19). In the present study, allergy to MPR occurred in 11.9% cases (8.7% women and 17.4% men). Allergy to MPR is much more common in older people, especially in those with eczema of the lower limbs or with leg ulcers. Machet *et al*. found the occurrence of MPR allergy among patients with leg ulcers to be 40% (20).

As allergy to topical steroids is much more common than previously thought, contact allergy to corticosteroids represents a significant therapeutic problem in the treatment of such chronic dermatoses as contact dermatitis. Clinical studies indicate that hypersensitivity to corticosteroids is becoming ever more common. Boffa *et al*. note that 5.98% of studied patients with contact eczema were allergic to one or more corticosteroids. The most common sensitivity was to tixocortol pivalate (4.5%), while 91.3% of corticosteroid-allergic subjects were found to be allergic to a combination of tixocortol pivalate and budesonide (21). A Mayo Clinic study reports that 10.69% of studied patients had an allergic reaction to at least one corticosteroid, with the most common sensitivities being to tixocortol pivalate (5.03%) and 0.1% budesonide (3.07%) (8). Such a high percentage of patients with allergy to corticosteroids in our study may be explained by the fact that all of these patients were adults (mean age 50.4) with a long duration of contact eczema (mean 6.9 years) and several years of experience applying topical corticosteroids (mean 4.2 years). Contact hypersensitivity to steroids was diagnosed in 12.3% of subjects with disease duration equal to or less than 5 years and in 18.9 % of patients with disease duration longer than 5 years, thus indicating that the risk of allergy to glucocorticosteroids increases with the duration of the disease.

In the present study, the corticosteroids included in the European Baseline Series, i.e. tixocortol-21-pivalate and 0.01% budesonide, a diagnostic allergen

Table 5. Prevalence of allergy to the group of steroids according to topical steroid used

Number of patients used steroids from group:	Positive reaction to steroids group									
	A		B		C		D1		D2	
	No.	%	No.	%	No.	%	No.	%	No.	%
A (n=74)	5	6.8	15	20.3	9	12.2	12	16.2	12	16.2
B (n=30)	1	3.3	6	20.0	4	13.3	4	13.3	5	16.7
C (n=12)	0	0.0	3	25.0	2	16.7	3	25.0	2	16.7
D1 (n=89)	4	4.5	18	20.2	10	11.2	14	15.7	13	14.6
D2 (n=40)	2	5.0	8	20.0	5	12.5	7	17.5	6	15.0

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for the B and D corticosteroid groups (22), identified 86.4% cases of steroid allergy. Tixocortol pivalate is a group A steroid and regarded as the best marker of allergy to hydrocortisone (22). Hypersensitivity to one steroid was observed in 36.4% of patients, and more than one in the remaining 63.7%. The most frequently obtained cross-reactions were between corticosteroids of groups B and D. As budesonide gives very frequent cross-reactions, it is regarded as one of the best markers of contact allergy to steroids; in this study, it identified 81.2% of patients with hypersensitivity to corticosteroids.

The concentration which should be used for corticosteroid allergen patch tests has not been determined. Some reports suggest that a high corticosteroid concentration increases allergen penetration, thus enabling effective demonstration of hypersensitivity despite its strong anti-inflammatory effect, whereas others note that lower concentrations allow a hypersensitivity reaction to be obtained more quickly (23). The results of the present study indicate that in 72.2% of cases both 0.1% and 0.01% budesonide gave a positive result, compared with 16.7% of cases with only 0.01% budesonide and 11.1% of cases with 0.1% budesonide, suggesting that the steroid allergen is more sensitive at a lower concentration.

In addition, 72.7% of patients with hypersensitivity to corticosteroids were also sensitized to non-steroidal haptens included in the European Baseline Series. These results confirm that polyvalent contact allergy to non-steroidal allergens is a risk factor for hypersensitivity to steroids. Reitamo reports that patients suffering from chronic dermatoses, and those who experience two or more positive tests with non-steroidal haptens, are at an increased risk of allergy to corticosteroids (24). Increased incidence of allergy to steroids also occurs in patients with chronic eczema, atopic dermatitis, and leg ulcers (25). Contact allergy to glucocorticosteroids may affect 12.8% of patients with atopic dermatitis, 20% of patients with chronic eczema, and 40% of patients with chronic leg ulcers (25,26). In the present study, changes on the lower limbs occurred in 40.9% patients with corticosteroid allergy.

CONCLUSION

There is no doubt contact allergy to corticosteroids represents a significant therapeutic problem in the treatment of chronic inflammatory dermatoses. Hypersensitivity to a topical corticosteroid should be suspected when dermatitis fails to respond to topical corticosteroid therapy or when it worsens during treatment. Factors that increase the risk of contact allergy to corticosteroids include the chronicity of the disease and coexistence of polyvalent contact allergy to non-steroidal haptens. In the case of polyvalent allergy to corticosteroids of different groups, topical steroid should be chosen from the group for which there is no hypersensitivity.

References:

1. Krasteva M, Kehren J, Ducluzeau MT, Sayag M, Cacciapuoti M, Akiba H, *et al*. Contact dermatitis I. Pathophysiology of contact sensitivity. Eur J Dermatol 1999;9:65-77.
2. Bordel-Gomez MT, Miranda-Romero A, Castrodeza-Sanz J. Epidemiology of contact dermatitis: prevalence of sensitization to different allergens and associated factors. Actas Dermosifiliogr 2010;1:59-75.
3. Rudzki E, Rebandel P, Grzywa Z. Certain properties of contact dermatitis in Poland. Inter Rev Allergol Clin Immunol 1997;3:71-5.
4. Burckhardt W. Klinische und therapeutische kurzberichte. Hautarzt 1959;10:42-3.
5. Kooij R. Hypersensitivity to hydrocortisone. Br J Dermatol 1959;71:392-4.
6. Mimesh S, Pratt M. Allergic contact dermatitis from corticosteroids: reproducibility of patch testing and correlation with intradermal testing. Dermatitis 2006;17:137-42.
7. Goossens A, Matura M. Contact allergy to corticosteroids. Allergy 2000;55:698-704.
8. Davis MD, el-Azhary RA, Farmer SA. Results of patch testing to a corticosteroids series: a retrospective review of 1188 patients during 6 years at Mayo Clinic. J Am Acad Dermatol 2007;56:921-7.
9. Rudzki E. Evolution of contact allergy in Poland (from CMEA to EU) (Polish) Alergia Astma Immunologia Kliniczna 2005;2:53–7.
10. Uter W, Hegewald J, Aberer W, Ayala F, Bircher AJ, Brasch J, *et al*. The European standard series in 9 European countries, 2002/2003 - First results of the European Surveillance System on Contact Allergies. Contact Dermatitis 2005;53:136-45.
11. Schäfer T, Böhler E, Ruhdorfer S, Weigl L, Wessner D, Wichmann HE, *et al*. Epidemiology of contact allergy in adults. Allergy 2001;56:1192-6.
12. Jensen CS, Lisby S, Baadsgaard O, Volund A, Menne T. Decrease in nickel sensitization in a Danish schoolgirl population with ears pierced after implementation of a nickel exposure regulation. Br J Dermatol 2002;146:636-42.
13. Kornik R, Zug KA. Nickel. Dermatitis 2008;19:3-8.

14. Piaserico S, Larese F, Recchia GP, Corradin MT, Scardigli F. Allergic contact sensitivity in elderly patients. Aging Clin Exp Res 2004;16:221-5.
15. Balato A, Balato N, Di Costanzo L, Ayala F. Contact sensitization of older patients in an academic department in Naples, Italy. Dermatitis 2008;19:209-12.
16. Turčić P, Marinović Kulišić S, Lipozenčić J. Patch test reactions to metal salts in patients with different types of dermatitis. Acta Dermatovenerol Croat 2013;21:180-4.
17. Torres F, Gracas M, Melo M, Tosti A. Management of contact dermatitis due to nickel allergy: an update. Clin Cosmet Investig Dermatol 2009;2:39-48.
18. Carlsen BC, Andersen KE, Menné T, Johansen JD. Patients with multiple contact allergies: a review. Contact Dermatitis 2008;58:1–8.
19. Avalos-Peralta P, García-Bravo B, Camacho FM. Sensitivity to Myroxylon pereirae resin (balsam of Peru). A study of 50 cases. Contact Dermatitis 2005;52:304-6.
20. Machet L, Couhé C, Perrinaud A, Hoarau C, Lorette G, Vaillant L. A high prevalence of sensitization still persists in leg ulcer patients: a retrospective series of 106 patients tested between 2001 and 2002 and a meta-analysis of 1975-2003 data. Br J Dermatol 2004;150:929-35.
21. Boffa MJ, Wilkinson SM, Beck MH. Screening for corticosteroid contact hypersensitivity. Contact Dermatitis 1995;33:149-51.
22. Matura M, Goosens A. Contact allergy to corticosteroids. Allergy 2000,55:698-704.
23. Chowdhury MMU, Statham BN, Sansom JE, Foulds IS, English JSC, Podmore P, *et al*. Patch testing for corticosteroid allergy with low and high concentrations of tixocortol pivalate and budesonide. Contact Dermatitis 2002;46:311-2.
24. Reitamo S, Lauerma AI, Stubb S, Käyhkö K, Visa K, Förström L. Delayed hypersensitivity to topical corticosteroids. J Am Acad Dermatol 1986;14:582-9.
25. Żmudzińska M, Czarnecka-Operacz M, Silny W. Contact allergy to glucocorticosteroids in patients with chronic venous leg ulcers, atopic dermatitis and contact allergy. Acta Dermatovenerol Croat 2008;16:72-8.
26. Kot M, Bogaczewicz J, Kręcisz B, Woźniacka A. Contact hypersensitivity to haptens of the European Standard Series and Corticosteroid Series in the population of adolescents and adults with atopic dermatitis. Dermatitis 2014;25:72-6.