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ORIGINAL ARTICLE

Periocular dermatitis: a report of 401 patients

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Abstract

Background Periocular contact dermatitis may appear as contact conjunctivitis, contact allergic and/or irritative eyelid and periorbital dermatitis, or a combination of these symptoms. The clinical symptoms may be induced by several environmental and therapeutic contact allergens.

Objectives The aim of the present study was to map the eliciting contact allergens in 401 patients with periocular dermatitis (PD) by patch testing with environmental and ophthalmic contact allergens.

Methods Following the methodics of international requirements, 401 patients were tested with contact allergens of the standard environmental series, 133 of 401 patients with the *Brial* ophthalmic basic and supplementary series as well.

Results Contact hypersensitivity was detected in 34.4% of the patients. Highest prevalence was seen in cases of PD without other symptoms (51.18%), in patients of PD associated with ophthalmic complaints (OC; 30.4%), and PD associated with atopic dermatitis (AD; 27.9%). In the subgroup of PD associated with seborrhoea (S) and rosacea (R), contact hypersensitivity was confirmed in 17.6%. Most frequent sensitisers were nickel sulphate (in 8.9% of the tested 401 patients), fragrance mix I (4.5%), balsam of Peru (4.0%), paraphenylendiamine (PPD) (3.7%), and thiomersal (3.5%). By testing ophthalmic allergens, contact hypersensitivity was observed in nine patients (6.7% of the tested 133 patients). The most common confirmed ophthalmic allergens were cocamidopropyl betaine, idoxuridine, phenylephrine hydrochloride, Na chromoglycinate, and papaine.

Limitations Patients with symptoms of PD were tested from 1996 to 2006.

Conclusions The occurence of contact hypersensitivity in PD patients was in present study 34.4%. A relatively high occurence was seen in cases of PD without other symptoms, in PD + OC and in PD + AD patients. The predominance of environmental contact allergens was remarkable: most frequent sensitizers were nickel sulphate, fragrance mix I, balsam of Peru, thiomersal, and PPD. The prevalence of contact hypersensitivity to ophthalmic allergens did not exceed l.5%.

Introduction and background

Periocular contact dermatitis may occur as contact conjunctivitis, allergic and/or irritative eyelid, periorbital dermatitis, or as a combination of these symptoms. Different skin diseases may induce similar symptoms in this area, and allergic and irritative dermatitis can elicit further isomorphic skin reactions. Skin diseases manifesting in the region [e.g. psoriasis, atopic dermatitis (AD), seborrhoeic dermatitis (S), rosacea (R)] can be associated with irritative or allergic contact sensitization. Bacterial and fungal infections can also modify the clinical picture. The very thin dermis of this region (0.55 mm – compared with other facial areas about 2 mm) predisposes the development of irritative and/or allergic skin reactions. The increased skin penetration is characteristic in the periocular region and can mainly be observed in females, children, and in the elderly.[1–3]

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Periocular dermatitis (PD) may be induced by several environmental contact allergens; therefore, one should consider cosmetics first.[4–6] Constituents irritating and allergising in mascaras and eye shadows are resins, colophony, solvents, glittering powders (aluminium, bismuth oxide, titanium), volatile oils and perfumes, lanalcolum, antioxidants, preservatives (paraben esthers, phenylmercuriacetate, Quaternium, sodium sorbate, benzalkonium chloride), and blending substances (diisopropanolamine, propylenglycol).[7–15] Pigments [paraphenylendiamine (PPD), nickel, ferric oxide][12,16–23] can also be found in mascaras; the leadsulphite content of certain Indian conjunctival mascaras is also known.[24] Ingredients and additives of facial and eye creams may also provoke irritative and/or allergic symptoms in the periorbicular region. The importance of blending substances should be emphasized; the dermatitis-provoking effects can be observed mostly in AD patients.[1,5,25–27] The clinical symptoms of AD patients may be complicated often by microbial superinfections and sensitizations.[28,29] Constituents of hair care products, ingredients, and additives of nail polishes and artificial nail products may also provoke skin symptoms in this region – especially late allergic reactions. Immediate reactions may also develop, provoking extracutaneous (respiratory) reactions.[17,19,30–34]

Basic, active, and additive agents of ophthalmic preparations are known allergens of the periorbital region. Most frequent ophthalmic allergens are phenylephrine, betablockers, antibiotics, resorcine, pilocarpine, thiomersal, chloramphenicol, and antazoline.[35–39] PD as occupational skin disease can be mainly observed in dental, cosmetic, wood and food industry, and in animal husbandry.[40–42] Plants and herbs may also cause PD: in case of allergy, exposure to the powder, extractum, and/or the pollen of the particular plant provokes contact dermatitis of the region.[43,44]

Patients and methods

Four hundred one patients with symptoms of PD were tested from 1996 to 2006 in the Allergological Laboratory and Consultation Unit of the Department for Dermatology, Venerology and Dermatooncology of Semmelweis University. The mean age of the patients was 49.9 years (range, 9–92). Three hundred thrity-nine of the patients (84.5%) were women (mean age: 51.2 years; range, 11–92) and 62 (15.5%) were men (mean age: 42.9 years; range, 9–84).

PD without other symptoms had 127 patients, PD + OC had 151 patients, PD + S, R had 74 patients, PD + AD had 43 patients, PD + P had 3 patients, PD + discoid lupus erythematosus (DLE) had 2 patients, and PD + PSS had 1 patient (Table 1).

The tests were performed with the allergens of the standard epicutan series (Table 2) and those of the Brial

Table 1 The diagnostic distribution of patients with PD

Diagnosis	*n* = 401	^{+}n = 138	%
PD without other symptoms	127	65	**51.18**
PD + OC	151	46	**30.4**
PD + AD	43	12	**27.9**
PD + S, R	74	13	**17.6**
PD + P	3	–	–
PD + DLE	2	1	
PD + PSS	1	1	

PSS, progressive systemic sclerosis.
^{+}n: number of patients with contact hypersensitivity.

Table 2 Contact hypersensitivity elicited by environmental allergens in the 401 patients

Allergens	^{+}n	%
Neomycin sulphate	3	0.7
Benzocaine	3	0.7
Iodchloroxochinolin	2	0.5
Paraben	3	0.7
Lanalcolum	7	1.7
Primin	–	–
Sesquiterpene lactone	2	0.5
Phenylbutazone	2	0.5
Potassium dichromate	2	0.5
Nickel sulphate	**36**	**8.9**
Cobalt chloride	8	2
TMTD	6	1,5
MBT	–	–
Colophony	7	1.7
Pix litantracis	9	2.2
Balsam of Peru	**16****	**4.0**
Turpentine	2	0.5
PPD	**15**	**3.7**
Hg(II)-amidochloride	7	1.7
Formaldehyde	6	1.5
IPPD	–	–
Propylene glycol	5	1.2
Thiomersal	**14**	**3.5**
Quaternium 15	1	0.25
Kathon CG	3***	0.7
Resorcin	–	–
Propolis	6	1.5
p-tert-butyl-phenol-formaldehyde-resin	1	0.25
Fragrance mix I.	**18**	**4.5**
Mercury chloride	7	1.7
Chloramphenicol	1	0.25
Chlorquinaldol	1	0.25

**: 8 contact urticaria, 1 contact urticaria + contact dermatitis.
***: 1 contact urticaria.
^{+}n: number of patients with contact hypersensitivity/allergen.
%: percentage of the examined 401 patients.

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Table 3 Ophthalmic contact allergens in PD + OC patients/Brial ophthalmic standard and supplementary series/(number of tested PD + OC patients = 133)

Allergens	v	+*n*	%
Cocamidopropyl betaine 1%	a.d.	2	**1.5**
Chlorpheniramine maleate 5%	p.	1	0.75
Benzalkonium chloride 0.1%	p.		
Atropinsulphate 1%	a.d.		
Idoxuridine 1%	p.	2	**1.5**
Phenylephrine hydrochloride 10% (Coca)	a.d.	2	**1.5**
Na-cromoglycinate 2%	p.	2	**1.5**
Na-ethylendiamine-tetraacetate 1%	p.		
Pilocarpine 1%	a.d.	1	0.75
Papaine 1%	p.	2	**1.5**
Acebutolol 2%	p.		
Pindolol 2%	p.		
Propranolol 2%	p.		
Amerchol L 101 50%	p.		
Polymixin-B-sulphate 3%	p.		
Na-disulphide 1%	p.		
Oxprenolol	p.		

v, vehicle; a.d., aqua destillata; p, petrolatum.
+*n*: number of patients with contact hypersensitivity/allergen.
%: percent of the examined 133 patients.

ophthalmic basic and supplementary series *(Brial Allergen GmbH, Greven)* (Table 3). Four hundred one patients were tested with contact allergens of the standard environmental series, 133 of 401 patients with the *Brial* ophthalmic series as well, following the methodics of international requirements.

Results

Contact hypersensitivity was confirmed in 138 of the 401 examined patients (34.4%). Highest percentage of hypersensitivity was seen in PD cases without other symptoms (51.18% of patients in the subgroup) and PD associated with ophthalmic symptoms (30.4%). The frequency of hypersensitivity was in PD + AD cases 27.9% and in PD + S, R cases 17.6%. Because of the low number of patients in the PD + P, PD + DLEm and PD + PSS subgroups, we don't assess these groups. We observed irritative skin reactions in 145 patients (Table 1).

Most frequent sensitizers were nickel sulphate (in 8.9% of the tested 401 patients), fragrance mix I (4.5%), balsam of Peru (4.0%), PPD (3.7%), and thiomersal (3.5%). Katon CG provoked contact urticaria in one patient. Balsam of Peru provoked contact urticaria in eight patients; in one patient, contact urticaria followed by eczematous reactions was soon provoked in 72 h (Table 2).

One hundred fifty-one of 401 patients had PD associated with OC (conjunctivitis chronica: 119 patients, blepharoconjunctivitis: 31 patients, and cornea ulcus: 1 patient). Onehundred thirty-three of them were tested with the ophthtalmic allergens as well. By testing ophthalmic allergens, contact hypersensitivity was confirmed in nine patients (6.79% of the tested 133 patients). A sensitization prevalence of 1.5% was confirmed by the following ophthalmic allergens: cocamidopropyl betaine, idoxuridine, phenylephrine hydrochloride, Na chromoglycinate, and papaine. A sensitization prevalence of 0.75% was observed by chlorpheniramine maleate and pilocarpine (Table 3).

Discussion

According to the literature patients patch tested due to symptoms of the periocular area are mostly diagnosed with allergic contact dermatitis, irritative contact dermatitis, AD, seborrhoeic dermatitis, and psoriasis. By AD, patients with PD symptoms can be observed positive to pach test reactions and contact allergies in a relative high percentage.[3,6,10,45] The prevalence of contact hypersensitivity in our 401 PD cases was 34.4%. A relatively high prevalence of contact hypersensitivity was seen in cases of PD without other symptoms (51.18%), in PD + OC (30.4%), and in PD + AD (27.9%) groups. Contact hypersensitivity was observed in 17.6% of the PD + S, R patients.

Nickel sulphate, cobalt chloride, fragrance mix, and antibiotics are the most common contact allergens in the periorbital region.[3,6,8,10,11,15,25,45] In our study, nickel sulphate, fragrance mix I, balsam of Peru, PPD, and thiomersal were the most frequent sensitizers (fig. 1). The leading role of nickel (36 patients, 8.9%) is not surprising considering the predominance of female patients. Concerning the region, the relevance can be questionable, but the exposure to the metal frames of spectacle, the nickel content of cosmetics, and the provoking effects of metal eyeliners should be considered.[12,20,21] The prevalence of hypersensitivity to fragrance mix I (4.5%) and balsam of Peru (4.0%) was to be expected according to the region. In compliance with current fashion, the periocular skin region is treated and made up with creams and cosmetics containing fragrances and herbal substances.[26,32] All of our affected patients used cosmetics and/or make ups. An increasing prevalence of PPD hypersensitivity (frequently seen as immediate reactions) has also been reported in the surveys of recent years.[6,16–19] The PPD containing make ups (eye liner, mascara) and hair dyes could be the ground of the relevance in our affected 15 patients. Regarding to therapeutical allergens, contact hypersensitivity to thiomersal should mainly be emphasized. According to our data and those of the literature, the prevalence of sensitization to ophthalmic allergens is below the prevalence of environmental allergens.[3,6,45] Its relevance, however, cannot be argued. Testing is recommended if definite anamnestic data are

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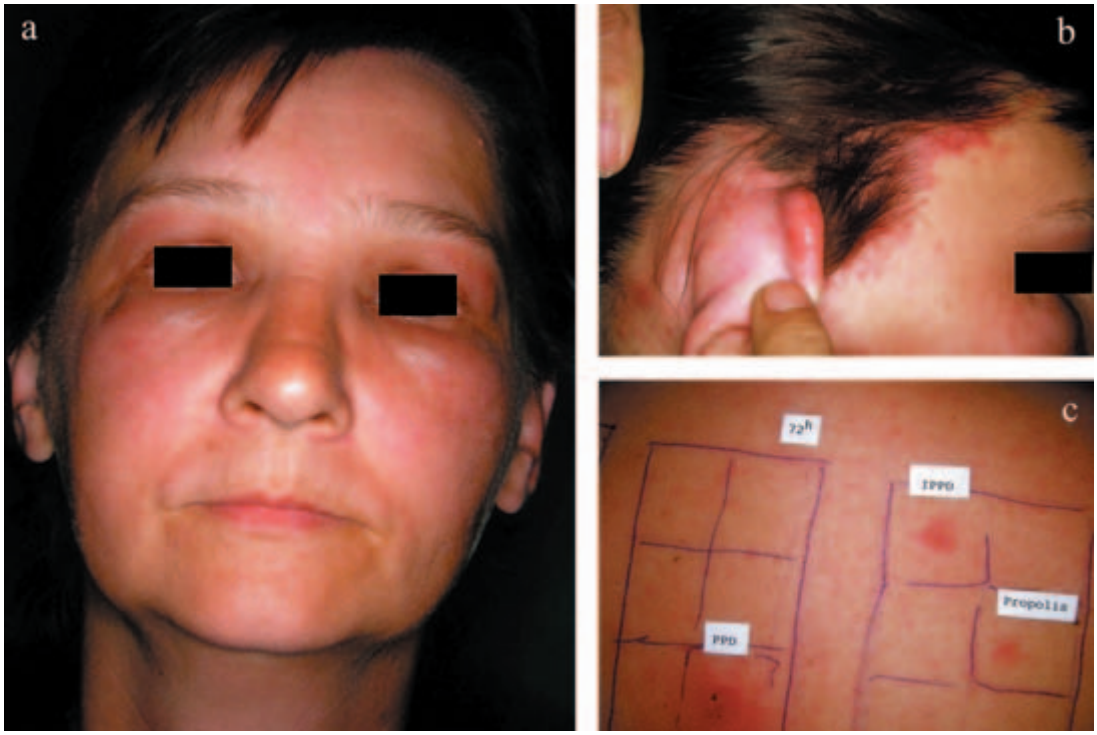

fig. 1 Clinical symptoms elicited by PPD-containing mascara and hair dye (a,b), and the reactions to skin tests, evaluated at 72 h (c).

fig. 2 Clinical symptoms of propylenglycol contact hypersensitivity.

fig. 3 Periocular manifestation of AD.

available. In our cases, all of the confirmed ophthalmic allergens were relevant, since the patients used local therapeutics or cosmetics containing the following sensitizers: cocamidopropyl betaine (shampoos, hair dyes, shower and bath gels), idoxuridine (eye drops, gels, ointments), phenylephrine hydrochloride (mydriatics, vasoconstrictors, alfa-1 receptor stimulants), Na chromoglycinate (anti-allergics), papaine (contact lens cleaners), chlorpheniramine maleate (antiallergics), and pilocarpine (eye drops).

Exposure to the suitable allergen is one of the issues of testing PD. Ophthalmic allergen series as well as test series of contact lens allergens and contact lens solution allergens may also be applied nowadays. However, the first test should be performed with the test series of the most common environmental allergens. It is essential to know the case history of the patient in order to ascertain the predisposing factors (atopy, psoriasis, seborrhoea, rosacea; figs 3 and 4) Patch testing for environmental allergens

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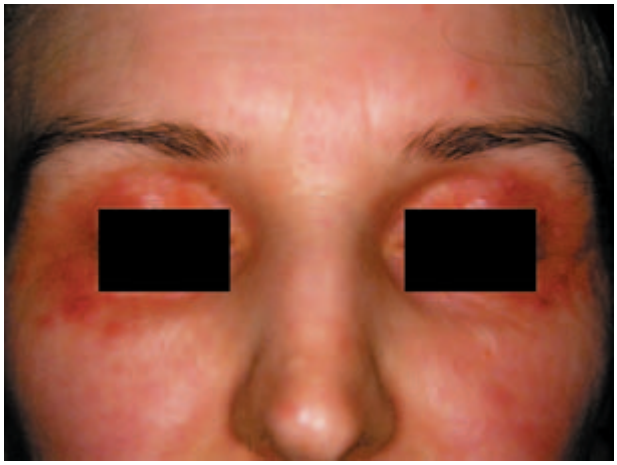

fig. 4 Manifestation of rosacea in the periocular region.

is recommended according to internationally accepted methodics; in cases of PD, evaluation on 5th and 7th days is of great significance. Some authors perform skin tests with the cosmetics in their original concentration, performing 'semi open' tests with mascaras or with liquid removers, allowing *in loco* testing as well.[26,45,46] To avoid false positive or irritative reactions, a 20-min waiting period before occlusion, 'semi open tests', or decrease of test concentrations are recommended. To avoid false negative reactions, 'use test' in the elbow folds or in the periocular region and patch tests *in loco* on the eyelids are also allowed.[8,26]

The most important factor for healing and prevention is the elimination of the allergens. The role of hands is important, since it may present an opportunity for the periocular region to be exposed to allergens not contacted directly with the face. After considering differential diagnostic possibilities and the elimination of the confirmed allergens, an allergen-free treatment is suggested in cases of PD. One should consider superinfections mainly in cases of AD.[1,27,29] The allergen-free therapy is a big challenge because a lot of ophthalmic preparations or creams may contain several contact allergens (fig. 2).

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