

Contact dermatitis from dipivefrine with possible cross-reaction to epinephrine

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A wide variety of topical ophthalmics are contact sensitizers (1, 2), including epinephrine hydrochloride (3–5). The development of dipivalyl epinephrine (dipivefrine), synthesised by the addition of 2 pivalic acid groups to epinephrine, results in a more lipophilic compound with greater penetration of the corneal layer and a lower incidence of side-effects than epinephrine, but with similar mydriatic effect on glaucoma (6, 7).

Case Report

A 68-year-old man with glaucoma had been treated for 3 years with Timofтол® 0.25% (timolol) and Glaurops® (dipivefrine) in his right eye and Timofтол® in the left. He presented with a 12-month history of eczema around the right eye, which had temporarily responded to topical corticosteroids. On examination, he showed a right-sided hyperaemic bulbar conjunctiva and oedematous and hyperpigmented periocular skin, with fine scaling. His left eye was not involved. After discontinuing Glaurops®, and treatment with topical corticosteroids, all lesions gradually cleared. Treatment with Timofтол® was continued with no adverse reactions. He gave no history of previous use of epinephrine.

Patch tests with the NACDG standard series, and with Glaurops® and Timofтол®, gave only a weak positive reaction to Glaurops® at D4 (Table 1). Patch testing the components of Glaurops® separately, using pet. and aq. as vehicles, elicited a strong reaction to dipivefrine 5% and 1% aq. at the D4. Only a weak reaction was

obtained to dipivefrine 5% pet. A patch test with epinephrine 1%, aq. (Adrenalina Llorente® 1:1000) was also positive at D4 (Table 1). 5 controls were negative to all tests.

Discussion

Among local adverse reactions to dipivefrine, burning sensation, pruritus, blurred vision, conjunctivitis, cystoid macular edema and ciliary body edema have all been described (6–11). Allergic contact dermatitis from dipivefrine has rarely been reported (12, 13). The positive reaction to epinephrine suggests cross-reactivity with dipivefrine, given their closely-related structures. Within the eye, dipivefrine is, in fact, de-esterified to epinephrine (14). Nevertheless, the injection of epinephrine in patients with contact sensitivity to epinephrine, in an emergency, has been deemed as safe (15). Our patch test results suggest that water is a better vehicle than petrolatum for dipivefrine.

References

- Herbst R A, Maibach H I. Contact dermatitis caused by allergy to ophthalmic drugs and contact lens solutions. *Contact Dermatitis* 1991; 25: 305–312.
- Grimalt F, Romaguera C. *Dermatitis de contacto*, 1st edition. Barcelona: Fontalba; 1987: 425–433.
- Becker B, Morton W R. Topical epinephrine in glaucoma suspects. *Am J Ophthalmol* 1996; 62: 272–277.
- Gibbs R C. Allergy contact dermatitis to epinephrine. *Arch Derm* 1970; 101: 92–94.
- Alani S D, Alani M D. Allergic contact dermatitis and conjunctivitis from epinephrine. *Contact Dermatitis* 1976; 2: 147–150.
- Kohn A N, Moss A P, Hargett N A, Ritch R, Smith H, Podos S M. Clinical comparison of dipivalyl epinephrine and epinephrine in the treatment of glaucoma. *Am J Ophthalmology* 1979; 87: 196–201.
- Kass M A, Mandell A I, Goldberg I, Paine J M, Becker B. Dipivefrine and epinephrine treatment of elevated intraocular pressure: a comparative study. *Arch Ophthalmol* 1979; 95: 1865–1866.
- Mills K B, Jacobs N A. A single-blind randomized trial comparing adrenaline 1.0% with dipivalyl epinephrine (Propine) 0.1% in the treatment of open-angle glaucoma and ocular hypertension. *Br J Ophthalmol* 1988; 72: 465–468.
- Liesegang T J. Bulbar conjunctival follicles associated with dipivefrin therapy. *Ophthalmology* 1985; 92: 228–233.
- Mehelas T J, Kollarits C R, Martin W G. Cystoid macular edema presumably induced by dipivefrin hydrochloride (Propine). *Am J Ophthalmol* 1982; 94: 682.
- Krieg P H, Schipper I. Drug-induced ciliar body oedema: a new theory. *Eye* 1996; 10: 121–126.
- Gaspari A A. Contact allergy to ophthalmic dipivalyl

Table 1. Patch test results

	D2	D4
NACDG standard series	—	—
Timofтол®	—	—
Glaurops®	—	+
Glaurops® components		
dipivefrine		
5% aq.	—	+++
1% aq.	—	++
5% pet.	—	+
1% pet.	—	—
manitol		
1% aq.	—	—
1% pet.	—	—
EDTA		
1% aq.	—	—
1% pet.	—	—
benzalkonium chloride		
1% aq.	—	—
1% pet.	—	—
epinephrine 1% aq.	—	++

epinephrine hydrochloride: demonstration by patch testing. *Contact Dermatitis* 1993; 28: 35–37.

13. Petersen P E, Evans R B, Johnstone M A, Henderson W R.. Evaluation of ocular hypersensitivity to dipivalyl epinephrine by component eye-drop testing. *J Allergy Clin Immunol* 1990; 85: 5: 954–958.

14. Wei C P, Anderson J A, Leopold I. Ocular absorption and metabolism of topically applied epinephrine and a dipivalyl ester of epinephrine. *Invest Ophthalmol Vis Sci* 1978; 17: 315–321.
15. Fisher A A. *Contact dermatitis*, 3rd edition. Philadelphia: Lea and Febiger; 1986: 141–166.

Nickel in tap water in Warsaw

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In 1983, studies in Copenhagen indicated that the nickel content of hot tap water in some flats was higher than that of cold water, but that in other flats, cold water contained a higher content of nickel than hot water (1). First samples of cold tap water collected in Leoben contained only 2 µg/100 ml, and first hot water samples contained up to 4 µg nickel/100 ml (2).

We had the opportunity to determine nickel content in the first 250 ml samples of tap water in 12 flats of

Warsaw-based doctors. In 5 flats, water pipes were made of metal; in 6 apartments, they were made of PVC; and in 1, they were made of mixed metal and PVC. Cold and hot water samples were examined by a spectrophotometric method based on the colour reaction of nickel with dimethylglyoxime (Spectroquant test, Merck). The detection limit was 5 µg/l. Results are depicted in Table 1.

It should be stressed that, in the case of metal water pipes, mean nickel content in hot water was higher than in cold water, and for pipes made of PVC, the mean nickel content was higher in cold water. Only a single flat had metal/PVC pipes installed. Results of water analysis from that particular apartment deviated greatly from the other samples. This flat was different from the others, as it was rarely used. The maximum limit for nickel content in drinking water in Poland stands at 30 µg/l (3). Our data indicate that the material water pipes are made of is the reason behind differences in nickel content of hot and cold water.

Table 1. Nickel content of tap water from flats in Warsaw (µg/l)

Delivery system	Flats	Cold water	Hot water
metal pipes	1	<5	<5
	2	5	15
	3	5	30
	4	12	5
	5	15	15
	mean	8.4	14
PVC pipes	1	55	<5
	2	5	5
	3	5	5
	4	20	10
	5	20	15
	6	40	15
	mean	15.8	9.1
metal/PVC pipes	1	1220	66

References

1. Andersen K E, Nielsen G D, Flyvholm M, Fregert S, Gruvberger B. Nickel in tap water. *Contact Dermatitis* 1983; 9: 143.
2. Lindemayr H. Friseurekzem und Nickelallergie. *Der Hautarzt* 1984; 35: 292–297.
3. Polish Ministry of Health and Social Welfare, regulation no. 35, 4 May 1990.