

Case Report

Anaesthetists should be aware of delayed hypersensitivity to phenylephrine

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Delayed reactions to phenylephrine, used as a mydriatic agent during ophthalmological surgical procedures, are well known. We diagnosed a delayed hypersensitivity reaction to phenylephrine included in an ophthalmic insert in a woman presenting, 24 h after surgery, with an acute blepharoconjunctivitis associated with eyelid eczema of the operated eye. The diagnosis was supported by the recognition of clinical symptoms associated with a positive patch test to phenylephrine.

Patients who present with previous contact eczema to phenylephrine may develop a generalized eczema if phenylephrine is injected intravenously. Intravenous phenylephrine is increasingly being used in the operating room to treat hypotension. This case report confirms the need for systematic allergological investiga-

tion of all drugs and substances administered during the peri-operative period in order to avoid a delayed hypersensitivity reaction occurring after the peri-operative period. Anaesthetists should be aware of the possibility of delayed hypersensitivity reactions involving phenylephrine.

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ADVERSE reactions to the administration of mydriatic eyedrops are not uncommon. The sensitizing potential of phenylephrine, used as a mydriatic and cycloplegic agent in ophthalmology, is well known (1). We report a case of a delayed hypersensitivity reaction following an ophthalmological surgical procedure in which the allergenic determinant responsible was phenylephrine.

Materials and methods

A 70-year-old woman was scheduled for ambulatory left cataract surgery. She denied any allergy to food, drugs or latex. Before surgery, cethexonium (Bactyl[®], Monaco, France) antiseptic eyedrops were instilled twice a day for 48 h. In the operating room before surgery, ocular and peri-ocular disinfection was performed with povidone-iodine (Betadine[®], Merignac, France, 5% solution for eye irrigation). Local anaesthesia was obtained with lidocaine gel (Xylocaine[®], Rueil Malmaison, France, 2% urethral gel) and oxybuprocaine (Cebesine[®], Montpellier, France, 0.4%). Immediately after, a phenylephrine and tropicamide ophthalmic insert (Mydriaser[®], La Rochelle, France)

was applied to the left cornea to obtain maximum pupillary dilatation. Anaesthesia and surgery were uneventful. After surgery, two further eyedrops were instilled into the left eye: befunolol (Bentos[®], Monaco, France) and dexamethasone and neomycin (Dexagran[®], La Rochelle, France). Beginning on the day after surgery, the patient was asked to instill a combination of three other eyedrops: indomethacin (Indocollire[®], Montpellier, France, 0.1%), ofloxacin (Exocine[®], Mougins, France, 0.3%) and dexamethasone and neomycin (Chibrocadron[®], Clermont-Ferrand, France). Twenty-four hours after surgery, the patient presented with an acute blepharoconjunctivitis associated with eyelid eczema of the operated eye. The same day, with the patient's consent, an allergological assessment was performed to identify the agent responsible.

Results

Patch tests to all molecules (cethexonium, povidone-iodine, lidocaine, oxybuprocaine, phenylephrine, tropicamide, befunolol, dexamethasone and neomycin) used during the peri-operative period were

performed, as well as patch tests to the preservatives (benzalkonium chloride, mercurothiolate) included in the three eyedrops and to methacrylate included in the insert. Prick tests to two latex extracts (Allerbio[®], Varennes-in-Argonne, France; Stallergènes[®], Paris, France) and patch tests to thiuram mix and mercapto mix were also performed.

Skin tests were performed according to the method of Lachapelle and Tennstedt (2) for patch tests and the standardized procedures recommended by the French Society of Anaesthesiology and Critical Care Medicine (3) for prick tests to latex. Prick tests to latex were read after 20 min, whereas patch tests to undiluted substances (cethexonium, povidone-iodine, lidocaine, oxybuprocaine, tropicamide, befunolol, dexamethasone, neomycin, benzalkonium chloride, mercurothiolate, methacrylate, thiuram mix and mercapto mix) were read at 48 h. All of the patch tests (Table 1) and prick tests to latex were negative, but the patch test to phenylephrine without preservatives was highly positive with a bullous eczema reproducing the clinical reaction. The ocular symptoms were relieved in 7 days with cortisone ointment.

Discussion

The clinical symptoms and allergological assessment confirmed the onset of a delayed hypersensitivity reaction to phenylephrine. The clinical arguments were as follows: (i) the delay in onset between the application of the insert and the reaction; (ii) symptoms typical of a delayed hypersensitivity mechanism (eczema and oedema). The allergological arguments were as follows: (i) the negative skin tests to cethexonium, povidone-iodine, lidocaine, oxybuprocaine, tropicamide, befunolol, dexamethasone,

neomycin, preservatives, methacrylate and latex; (ii) the positive patch test to phenylephrine confirming its responsibility and the T-cell-mediated mechanism of the reaction.

Delayed hypersensitivity reactions to phenylephrine following ophthalmological procedures are known complications (4–7), which are rarely located at sites other than the peri-ocular region (8). Patients are capable of sensitization at any age (1); indeed, a case of allergic contact conjunctivitis has been reported in a neonate exposed to mydriatics (9). In the operating room setting, α -agonists, such as phenylephrine, are increasingly being used to treat peri-operative hypotension or to maintain maternal arterial pressure during spinal anaesthesia (10–12). Although delayed hypersensitivity reactions following intravenous phenylephrine injection during the peri-operative period have not yet been reported, caution should be taken in patients with a previous history of delayed hypersensitivity reactions following phenylephrine. In these circumstances, the evaluation of the risk/benefit ratio of intravenous phenylephrine administration should probably be taken into consideration, as there is a risk that patients may develop a generalized eczema if phenylephrine is injected intravenously (13, 14). Therefore, it would be prudent to replace phenylephrine with another vasopressor in these cases, as cross-reactivity with closely related and structurally similar drugs, such as epinephrine and ephedrine, has not been established (5, 15).

This case report confirms the need for systematic allergological investigation of all drugs and substances administered by the anaesthetist and surgeon during the peri-operative period in order to avoid delayed hypersensitivity reactions. This systematic investigation should also consider preservatives, which are known to induce such delayed reactions. Anaesthetists should be aware of delayed hypersensitivity reactions to phenylephrine.

Table 1

Allergological assessment.

	Patch test
Cethexonium	–
Povidone-iodine	–
Lidocaine	–
Oxybuprocaine	–
Phenylephrine	+++
Tropicamide	–
Befunolol	–
Dexamethasone	–
Neomycin	–
Thiuram mix	–
Mercapto mix	–
Benzalkonium chloride	–
Mercurothiolate	–
Methacrylate	–

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