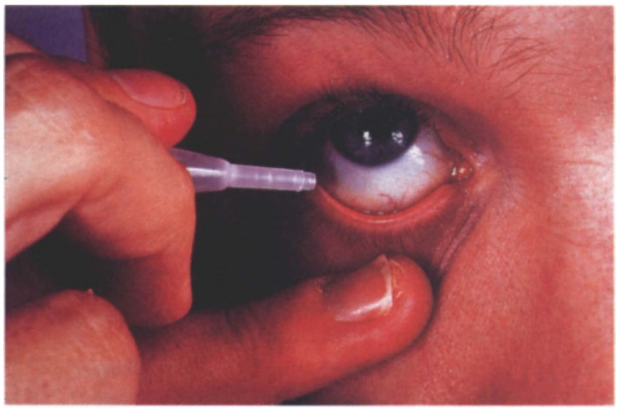

Fig. 2. *Eye drop application technique using the right middle finger to hold the lower eyelid down.*

During a holiday the signs and symptoms began to resolve, recurring and progressing rapidly on returning to work, which suggested an allergy to a work product.

She consulted a dermatologist, who confirmed an allergic contact dermatitis. Patch testing showed a 1+ result to proxymetacaine eye drops 0.5% at days 2 and 4. She had regularly used these since 1994. Positive allergic responses were also found to neomycin 20% in petrolatum (pet.), gentamicin 20% pet., thiomersal 0.10% pet. and isoeugenol 2.0% pet. in the fragrance mix. These were felt to be either of past or unknown relevance. Patch tests to other local anaesthetics including amethocaine 5.0% pet., lignocaine 5.0% pet. and oxybuprocaine eye drops 0.4% were negative.

She stopped using the proxymetacaine eye drops and treatment with betamethasone valerate ointment (Betnovate) was commenced. She changed to using oxybuprocaine eye drops as a first choice, which she had used regularly since 1979 with no problems. The skin had significantly improved within 2 weeks, although 12 months after the first symptoms the finger remains sensitive and prone to breaking down and the skin at the nail bed remains swollen. There is persistent deformity of the nail.

Comment

Fingertip allergic contact dermatitis secondary to eye drops occurring in an ophthalmologist has very rarely been reported. March and Greenwood[1] and more recently Liesegang and Perniciaro[2] have previously reported fingertip allergic contact dermatitis to proxymetacaine (proparacaine). In the latter report it took almost 3 years to diagnose the problem, because the allergen was not included in the original patch test series. The ophthalmologist affected was subjected to treatment with oral prednisolone, methotrexate and ultraviolet B phototherapy in an attempt to treat the condition before the nature of the allergen was recognised.

In this case the diagnosis was delayed for 4 months, because the association with the frequently used proxymetacaine eye drops was not immediately recognised. The ophthalmologist had been using the eye drops for over 4 years without any problems, but since the underlying pathogenesis is one of delayed hypersensitivity, previous continued exposure is a prerequisite. Proxymetacaine is an ester-type local anaesthetic and fortunately no cross-reacting or coexisting allergy to the other ester- or amide-type local anaesthetics has been elicited in this case. Allergic contact dermatitis to the active ingredients and preservatives in ophthalmic solutions is not uncommonly seen affecting the eye and eyelids of patients.[3–5] It appears to occur very rarely in practising ophthalmologists. Specialists with chronic hand eczema should have patch testing performed, otherwise the diagnosis of allergic contact dermatitis will be delayed and this may affect clinical practice.

References

1. March C, Greenwood MA. Allergic contact dermatitis to proparacaine. Arch Ophthalmol 1968;79:159–60.
2. Liesegang TJ, Perniciaro C. Fingertip dermatitis in an ophthalmologist caused by proparacaine. Am J Ophthalmol 1999;127:240–1.
3. Marsh RJ, Towns S, Evans KF. Patch testing in ocular drugs allergies. Trans Ophthalmol Soc UK 1978;98:278–80.
4. Aoki J. Allergic contact dermatitis due to eye drops: their clinical features and the patch test results. Nippo Ika Daigaku Zasshi 1997;64:232–7.
5. Herbst RA, Maibach HI. Contact dermatitis caused by allergy to ophthalmic drugs and contact lens solutions. Contact Dermatitis 1991;25:305–12.

C.E. Riddell[1]
J. Reed[2]
S. Shaw[2]
J. Duvall-Young[1]
[1]Department of Ophthalmology
Wycombe Hospital
High Wycombe
Bucks, UK
[2]Department of Dermatology
Amersham Hospital
Amersham
Bucks, UK

Claire Riddell ✉
Oxford Eye Hospital
Woodstock Road
Oxford OX2 6HE, UK

Sir,

Brimonidine tartarate 0.2% (Alphagan) associated granulomatous anterior uveitis

Brimonidine tartarate is a new topically acting α_2 adrenergic receptor agonist used in the management of primary open angle glaucoma and ocular hypertension. Here we report a case of granulomatous anterior uveitis following its use as an adjunctive therapy in a patient with ocular hypertension who was treated with betaxolol and pilocarpine for 3 years.

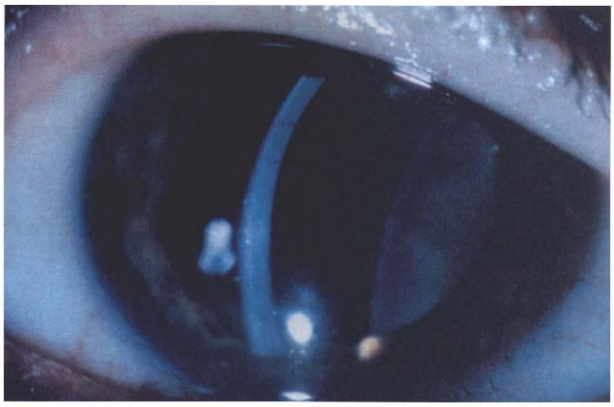

Fig. 1. *Anterior segment photograph of the left eye showing keratic precipitates with cells and flare.*

Case report

A 73-year-old woman who was a known ocular hypertensive for past 3 years, was reviewed in the eye clinic as a part of her 6 monthly check-up. Her medication included betaxolol (0.5%) b.d. and pilocarpine (2%) q.d.s. in both eyes. Her intraocular pressure (IOP) was found to be 24 mmHg in the right eye and 30 mmHg in the left on Goldmann applanation tonometry and pilocarpine was changed to brimonidine 0.2% (Alphagan; Allergan, High Wycombe) b.d. to achieve better control of IOP. On her next visit after 2 months the IOP was within normal limits.

Six months later she presented to the eye clinic with complaints of severe redness and blurring of vision for 2 months prior to her visit, for which she had been treated by her general practitioner with topical antibiotics. On examination her vision had decreased from 6/6 in both eyes to 6/18 in the right eye and 6/9 in the left. She had ciliary congestion, bilateral scattered mutton fat keratic precipitates with cells and flare (++) and an IOP of 34 mmHg in both eyes (Fig. 1). Examination of both fundi revealed clear vitreous with no posterior segment activity. A diagnosis of bilateral anterior uveitis was made and she was treated with topical dexamethasone (0.1% q.d.s.), the condition resolving uneventfully in a month.

The eye condition recurred again a month after stopping topical steroids. A uveitis screening test including blood tests (full blood count, ESR, angiotensin converting enzyme, syphilis serology) and chest radiograph proved negative. This raised the possibility of drug-induced uveitis and brimonidine 0.2% was then thought to be the offending agent as this drug was the latest addition to her local therapy. Subsequently the brimonidine 0.2% was discontinued and she was treated with topical dexamethasone (0.1% q.d.s.) as before with complete resolution in 2 weeks.

A brimonidine 0.2% challenge test was performed to her left eye after obtaining informed consent. She developed redness in that eye (Fig. 2) after 4 days of drug usage and examination disclosed a unilateral granulomatous anterior uveitis. The right eye was entirely normal. The challenge test was terminated and

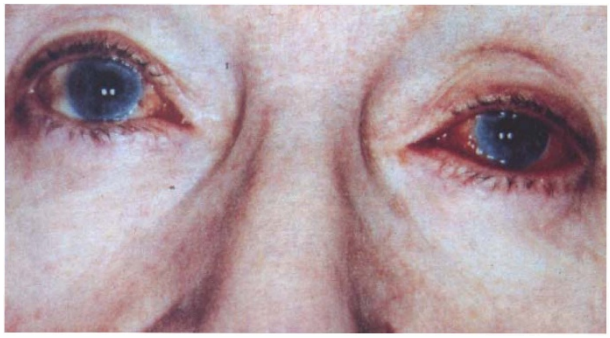

Fig. 2. *Recurrence of inflammation in the left eye after a brimonidine 0.2% challenge test.*

patient was treated with topical steroids, which resulted in complete resolution of uveitis with no sequelae within 2 weeks.

Comment

The common ocular side-effects of brimonidine 0.2% include hyperaemia, burning and conjunctival follicles. Occasional side-effects include photophobia, corneal erosions and staining and conjunctivitis.[1]

This case represents a new clinical observation of anterior uveitis associated with the use of brimonidine 0.2%. This drug, being an α_2 agonist, has a dual mechanism of action:[2] it decreases the production of aqueous and increases the outflow through the conventional pathway. The possible mechanism of induction of ocular inflammation remains speculative as it is difficult to achieve histopathological confirmation. Theoretically drugs cause uveitis by a direct or indirect mechanism.[3] Direct mechanisms require that the drug gains entry into the eye resulting in uveitis in 24–48 h. An indirect mechanism, however, results from stimulation of the immune system by the offending drug, resulting in formation of anti-drug antibodies. This may take weeks or months from initial exposure. As our patient presented a few months after starting the treatment, the mechanism is most likely to be immune-mediated rather than direct toxicity. The optical steroids suppressed the inflammation but this recurred on stopping the steroids. The recurrence of inflammation after rechallenge with brimonidine 0.2% further supports the association between uveitis and the drug. Though it is possible that the other components of the formulation may be responsible for the uveitis, we believe this is unlikely as the patient had tolerated various ocular medications in the past for a long period.

Anterior uveitis has been associated with topical beta blocker use,[4] and latanoprost.[5] Naranjo *et al.*[6] proposed seven criteria to establish causality of adverse events by drugs. Brimonidine tartarate in this case meets four of these. We believe this is the first case report of granulomatous uveitis following the use of topical brimonidine tartarate which led to the discontinuation of the drug. Clinicians need to be aware of this late-onset complication which occurs after a few months after

brimonidine usage with a secondary rise in IOP and responds well to stopping the drug and steroid eye drops.

References

1. British National Formulary. London: British Medical Association and The Royal Pharmaceutical Society of Great Britain, September 1999:469.
2. Toris CB, Gleason ML, Camras CB, *et al.* Effects of brimonidine on aqueous humor dynamics in human eyes. Arch Ophthalmol 1995;113:1514–7.
3. Moorthy RS, Valluri S, Jampol LM. Drug induced uveitis. Surv Ophthalmol 1998;42:557–70.
4. Melles R, Wong I. Metipranolol-associated granulomatous iritis. Am J Ophthalmol 1994;118:712–5.
5. Fechtner RD, Khouri AS, Zimmerman TJ, *et al.* Anterior uveitis associated with latanoprost. Am J Ophthalmol 1998;126:37–41.
6. Naranjo CA, Busto U, Sellers EM, *et al.* A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther 1981;30:239–45.

R. Goyal
A.R. Raghu Ram ✉
Department of Ophthalmology
Royal Glamorgan Hospital
Ynysmaerdy
Llantrisant
South Wales CF72 8XR, UK

Sir,

Pupil function after phacoemulsification and extracapsular cataract surgery

Nuclear expression during extracapsular cataract surgery is often associated with overstretching of the pupil sphincter. During extracapsular cataract extraction (ECCE), nucleus expression and insertion of larger-diameter posterior chamber intraocular lens (PC-IOL) implants can cause significant surgical trauma to the sphincter pupillae, particularly when the pupil is poorly dilated.

Phacoemulsification by means of *in situ* nuclear fragmentation and insertion of small-diameter PC-IOL avoids the need for nuclear expression and therefore peroperative iris trauma. This may result in better pupillary function post-operatively. Gibbens *et al.*[1] compared pupillary function after intracapsular and extracapsular surgery and found significantly compromised pupil function in the intracapsular group. Pupil function following phacoemulsification has not been the subject of much previous investigation.

We prospectively studied pupillary function after phacoemulsification and ECCE with PC-IOL implantation by measuring pupil diameters in dark and bright illumination and after 60 min of mydriasis with tropicamide 1% and phenylephrine 10% using static infrared photography. Twenty-nine eyes of 29 patients undergoing cataract surgery by phacoemulsification (20) or ECCE (9) were included. Exclusion criteria for the study were: previous intraocular inflammation, trauma, other intraocular surgery, presence of any ocular disorder and systemic disease or medication influencing pupil function. Accommodation was controlled by having the subjects fixate on a small illuminated target 6 m away.

An indirect ophthalmoscope provided the bright illumination. A Nikon camera with a 60 mm Nikon micro-lens was adapted to take static infrared photographs on a high-speed Kodak infrared film. The processed negatives were projected with an angioprojector at a ×10 magnification. A masked observer recorded pupillary diameters in horizontal and vertical meridians. An unpaired *t*-test was used for the comparison of the pupil diameters between the phacoemulsification and the ECCE group.

The mean age of the patients was 67.3 years and 70 years in the ECCE and phacoemulsification groups respectively. There was no significant difference between the pre-operative pupillary diameter in the two groups in the dark ($p = 0.4$) and light ($p = 0.2$) and after mydriasis ($p = 0.8$). Following phacoemulsification, the dilated pupil diameter was smaller (7.3 mm vs 6.9 mm, $p = 0.01$) compared with baseline. There was no significant change in the pupil diameter in the dark (4.6 mm vs 4.5 mm, $p = 0.71$) and the light (2.4 mm vs 2.5 mm, $p = 0.35$). Following ECCE, there was a significant difference in the dilated pupil diameter (7.2 mm vs 6.7 mm, $p = 0.03$) and in bright illumination (2.1 mm vs 2.7 mm, $p = 0.009$).

Intraocular surgery, though calculated and planned, may still subject the iris to various degrees of mechanical stress which may manifest itself as post-operative abnormalities of pupil shape and motility. This preservation of pupil constriction after phacoemulsification is probably due to reduced sphincter pupillae trauma peroperatively.

Both ECCE and phacoemulsification with intraocular lens implant result in a statistically significant reduction in maximal pupil dilation in response to mydriatic agents. The physiological pupil diameter in the dark is unaffected by surgery in either group of patients. Physiological pupil constriction in response to bright light is, however, significantly reduced after ECCE, whilst it remains preserved after phacoemulsification. The reduction in mydriatic pupil dilation post-operatively after ECCE is unlikely to be of clinical significance.

References

1. Gibbens MV, Goel R, Smith SE. Effect of cataract extraction on the pupil response to mydriatics. Br J Ophthalmol 1989;73:563–5.

Hooman Sherafat
Homayoun Tabandeh
Masoud Teimory
Ophthalmic Unit
St George's Hospital
London SW17 0QT, UK

Mr Masoud Teimory, FRCOphth ✉
Ophthalmic Unit
Worthing Hospital
Park Avenue
Worthing BN11 2DH, UK
e-mail: Teimory@aol.com
