Journal of the South East Asia Glaucoma Interest Group

Volume 9 Number 2 April 2007

Asian Journal of OPHTHALMOLOGY

Quality of Life of Patients with Glaucoma

Wavefront-guided Laser in Situ Keratomileusis

Blepharophimosis, Amblyopia, and Refractive Errors

Ocular Blood Flow Velocity and Resistive Index

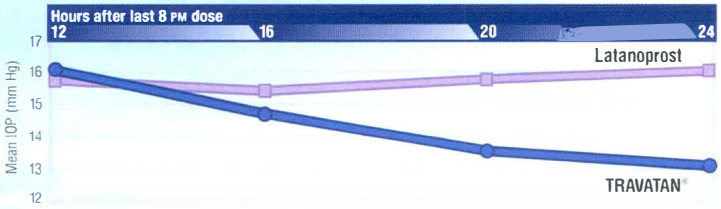
Herpes Simplex Virus Endotheliitis

Ultrasound Biomicrosopy of Uveal Tumours

Scientific Communications

Endurance

TRAVATAN® Solution is still going strong 24 hours post dose.[1*]



TRAVATAN®

(travoprost eye drops solution 0.004%)

Control That Lasts.

TRAVATAN® (travoprost 0.004%) Ophthalmic Solution Sterile **DESCRIPTION** Travoprost is a highly selective, potent agonist for the FP prostanoid receptor. Its chemical name is isopropyl (Z)-7-[(1*R*,2*R*,3*R*,5*S*)-3,5-dihydroxy-2-[(1*E*,3*R*)-3-hydroxy-4-[(α,α,α-trifluoro-*m*-tolyfloxy]-1 butenyl]cyclopentyl]-5-heptenoate. Its molecular formula is $C_{26}H_{35}F_3O_6$. Travoprost is a clear, colorless to pale yellow oil, which is very soluble in acetonitrile, methanol, octanol, and chloroform. It is practically insoluble in water. TRAVATAN® 0.004% Ophthalmic Solution is supplied as a sterile, buffered aqueous solution of travoprost with a pH of approximately 6.0 and an osmolality of approximately 290 mOsmol/kg. Each mL of TRAVATAN® 0.004% contains 40 µg travoprost. Preservative: benzalkonium chloride 0.015%. Inactive Ingredients: polyoxyl 40 hydrogenated castor oil, tromethamine, boric acid, mannitol, edetate disodium, sodium hydroxide and/or hydrochloric acid (to adjust pH) and purified water. **CLINICAL PHARMACOLOGY** Mechanism of Action Travoprost free acid is a highly selective, potent agonist for the FP prostanoid receptor. FP receptor agonists are reported to reduce intraocular pressure by increasing uveoscleral outflow. Pharmacokinetics/Pharmacodynamics Absorption: Travoprost is absorbed through the cornea. Studies in rabbits have shown peak concentrations in aqueous humor were reached one to two hours following topical administration. In humans, peak plasma concentrations of travoprost free acid were low (25 pg/mL or less) and occurred within 30 minutes following topical administration. Elimination: Ocular and systemic clearance of travoprost free acid is rapid, with a mean half-life of 45 minutes. Distribution: Travoprost free acid is rapidly and extensively metabolized to inactive metabolites. Biotransformations include beta-oxidation of the ω(carboxylic acid) chain to give the 1,2-dinor and 1,2,3,4-tetranor analogs, oxidation of the 15-hydroxyl moiety, as well as reduction of the 13,14 double bond. Excretion: In rats, 95% of a subcutaneous radiolabeled dose was eliminated within 24 hours. The major route of elimination was via the bile (61%) with the remainder excreted by the kidneys. **INDICATIONS AND USAGE** TRAVATAN® Ophthalmic Solution is indicated for the reduction of intraocular pressure in patients with open-angle glaucoma or ocular hypertension. **CLINICAL STUDIES** TRAVATAN® 0.004% Ophthalmic Solution dosed once-daily in patients with open-angle glaucoma or ocular hypertension produced significant reductions in intraocular pressure (IOP) when used either as primary therapy or adjunctively to TIMOPTIC® (timolol maleate ophthalmic solution) 0.5% BID. As primary therapy, TRAVATAN® 0.004%, dosed QD, reduced IOP 7 to 9 mmHg. Stable diurnal IOP reductions were achieved as early as 2 weeks after initiation of therapy and were maintained over the 6 to 12 month treatment periods in three (3) well-controlled studies. The IOP reductions with TRAVATAN® (travoprost 0.004%) Ophthalmic Solution were superior to those obtained with TIMOPTIC® and equal or better than those obtained with XALATAN® (latanoprost ophthalmic solution) 0.005% QD. TRAVATAN® 0.004% demonstrated an earlier stabilization of IOP reduction and better IOP control throughout the day compared to XALATAN® 0.005%. TRAVATAN® 0.004% was significantly more effective (up to 1.4 mmHg) than XALATAN® 0.005% in reducing IOP in black patients. A responder analysis (IOP reduction ≥30% or mean IOP ≤17 mmHg) demonstrated that TRAVATAN® 0.004% had a significantly higher responder rate (56%) compared to XALATAN® 0.005% (50%) and which were both significantly greater than TIMOPTIC® (40%). In a 6-month well-controlled study, TRAVATAN® 0.004% dosed QD adjunctively to TIMOPTIC® 0.5% BID provided additional clinically significant IOP reductions (6 to 7 mmHg). **CONTRAINDICATIONS** Known hypersensitivity to travoprost, benzalkonium chloride or any other ingredients in this product. TRAVATAN® may interfere with the maintenance of pregnancy and should not be used by women during pregnancy or by women attempting to become pregnant. **WARNINGS** TRAVATAN® may gradually change eye color, increasing the amount of brown pigmentation in the iris by increasing the number of melanosomes (pigment granules) in melanocytes. The long-term effects on the melanocytes and any consequences thereof are currently unknown. The change in iris color occurs slowly and may not be noticeable for months to years. These changes may be permanent. Periorbital and/or eyelid skin darkening has been reported in association with the use of TRAVATAN®. TRAVATAN® may gradually change eyelashes in the treated eye; these changes include: increased length, thickness, pigmentation, and/or number of lashes. Patients who receive treatment in only one eye may experience increased brown pigmentation of the iris, periorbital and/or eyelid tissue, and eyelashes in the treated eye. They may also experience disparity between the eyes in length, thickness, and/or number of eyelashes. These changes in pigmentation and lash growth may be permanent. **PRECAUTIONS** **General** There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products. These containers had been inadvertently contaminated by patients who, in most cases, had a concurrent corneal disease or a disruption of the epithelial surface (see Information for Patients). Patients may slowly develop increased brown pigmentation of the iris. This change may not be noticeable for months to years (see Warnings). This change in eye color has predominantly been seen in patients with mixed colored irides, i.e., blue-brown, grey-brown, yellow-brown and green-brown; however, it has also been observed in patients with brown eyes. Based upon information from the literature, the color change is believed to be due to increased melanin content in the stromal melanocytes of the iris. Typically, the brown pigmentation around the pupil spreads concentrically towards the periphery in affected eyes, but the entire iris or parts of it may become more brownish. No further increase in brown iris pigment has been observed after discontinuation of treatment, but the resultant color change may be permanent. TRAVATAN® should be used with caution in patients with active intraocular inflammation (iritis/uveitis). Macular edema, including cystoid macular edema, has been reported during treatment with prostaglandin $F_{2\alpha}$ analogues. These reports have mainly occurred in aphakic patients, pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema. TRAVATAN® (travoprost 0.004%) Ophthalmic Solution should be used with caution in these patients. Patients should remove contact lenses prior to administration of the solution. Lenses may be reinserted 15 minutes following administration of TRAVATAN®. **Information for Patients** Patients should be advised concerning all the information contained in the Warnings and Precautions sections. Patients should also be instructed to avoid allowing the tip of the dispensing container to contact the eye or surrounding structures because this could cause the tip to become contaminated by common bacteria known to cause ocular infections. Serious damage to the eye and subsequent loss of vision may result from using contaminated solutions. Patients also should be advised that if they develop an intercurrent ocular condition (e.g., trauma, or infections) or have ocular surgery, they should immediately seek their physician's advice concerning the continued use of the multi-dose container. Patients should be advised that if they develop any ocular reactions, particularly conjunctivitis and lid reactions, they should immediately seek their physician's advice. Patients should also be advised that TRAVATAN® contains benzalkonium chloride which may be absorbed by contact lenses. Contact lenses should be removed prior to administration of the solution. Lenses may be reinserted 15 minutes following administration of TRAVATAN®. If more than one topical ophthalmic drug is being used, the drugs should be administered at least five (5) minutes apart. **Carcinogenesis, Mutagenesis, Impairment of Fertility** Travoprost was not mutagenic in bacteria, in one mouse lymphoma assay, in the mouse micronucleus tests and in the rat chromosome aberration assay. In another mouse lymphoma assay, higher concentrations of travoprost were slightly mutagenic only in the presence of activation enzymes. In life and early post-mortem evaluations of carcinogenicity studies in rats and mice suggest no evidence of a carcinogenic potential. Travoprost did not affect mating or fertility indices in male or female rats at subcutaneous doses up to 10 µg/kg/day (250 times the recommended human dose). The mean number of corpora lutea was slightly reduced at that dose, and the post-implantation losses were increased, but was not affected at 3 µg/kg/day (75 times the maximum recommended human dose). **Pregnancy: Teratogenic Effects Pregnancy Category: C** In reproduction studies conducted in pregnant rats and mice, travoprost reduced fetal viability when administered during gestation at doses as low as 1.0 µg/kg/day (25 times the maximum recommended human dose) with the lowest no effect level at 0.3 µg/kg/day (7.5 times the maximum recommended human dose). The incidence of skeletal malformations was increased in fetuses of rat dams receiving travoprost by subcutaneous injection at 10 µg/kg/day (250 times the maximum recommended human dose), but not at 3 µg/kg/day (75 times the maximum recommended human dose). No fetal abnormalities were observed in mice at 1.0 µg/kg/day (25 times the maximum recommended human dose). No adequate and well-controlled studies have been performed in pregnant women. TRAVATAN® may interfere with the maintenance of pregnancy and should not be used by women during pregnancy or by women attempting to become pregnant. **Nursing Mothers** A study in lactating rats demonstrated that radiolabeled travoprost and/or its metabolites were excreted in milk. It is not known whether this drug or its metabolites are excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when TRAVATAN® is administered to a nursing woman. **Pediatric Use** Safety and effectiveness in pediatric patients have not been established. **Geriatric Use** No overall differences in safety or effectiveness have been observed between elderly and other adult patients. **ADVERSE REACTIONS (see Warnings and Precautions)** The most common ocular adverse event observed in controlled clinical studies with TRAVATAN® (travoprost 0.004%) Ophthalmic Solution was ocular hyperemia which was reported in 35 to 50% of patients. 95% of the ocular hyperemia observed with TRAVATAN® (travoprost 0.004%) Ophthalmic Solution was mild in intensity and subsided over time without treatment. Approximately 3% of patients discontinued therapy due to conjunctival hyperemia. Ocular adverse events reported at an incidence of 5 to 10% included decreased visual acuity, eye discomfort, foreign body sensation, pain, and pruritus. Ocular adverse events reported at an incidence of 1 to 4% included, abnormal vision, blepharitis, blurred vision, cataract, cells, conjunctivitis, dry eye, eye disorder, flare, iris discoloration, keratitis, lid margin crusting, photophobia, subconjunctival hemorrhage, and tearing. Nonocular adverse events reported at a rate of 1 to 5% were accidental injury, angina pectoris, anxiety, arthritis, back pain, bradycardia, bronchitis, chest pain, cold syndrome, depression, dyspepsia, gastrointestinal disorder, headache, hypercholesterolemia, hypertension, hypotension, infection, pain, prostate disorder, sinusitis, urinary incontinence, and urinary tract infection. **OVERDOSAGE** A single-dose intravenous study in rats was conducted to elucidate maximal acute hazard. The dose employed was 250,000-times the proposed daily clinical exposure and over 5000-times the possible exposure from the entire contents of one product container. No treatment related pharmacotoxic signs were present in the animals receiving Travoprost. If overdosage with TRAVATAN® occurs, treatment should be symptomatic. **DOSAGE AND ADMINISTRATION** The recommended dosage is one drop in the affected eye(s) once-daily in the evening. The dosage of TRAVATAN® should not exceed once-daily since it has been shown that more frequent administration may decrease the intraocular pressure lowering effect. Reduction of intraocular pressure starts approximately 2 hours after administration and the maximum effect is reached after 12 hours. TRAVATAN® may be used concomitantly with other topical ophthalmic drug products to lower intraocular pressure. If more than one topical ophthalmic drug is being used, the drugs should be administered at least five (5) minutes apart. **HOW SUPPLIED** TRAVATAN® (travoprost 0.004%) Ophthalmic Solution is a sterile, isotonic, buffered, preserved, aqueous solution supplied in Alcon's oval DROP-TAINER® package system inside a sealed foil pouch. This package system is comprised of a plastic oval shaped dispenser bottle, a dropper tip and tamper evident neck-band which shrinks to conform around the closure and neck area of the package. 0.004%: 2.5 mL fill. **Storage** Store between 2° to 25° C (36° to 77° F). Refrigeration is not required. Rx Only (USA) **CAUTION:** Federal (USA) law prohibits dispensing without prescription.

*TIMOPTIC is a registered trademark of Merck & Co., Inc. †XALATAN is a registered trademark of Pharmacia Corp. U.S. Patent Nos. 5,631,287; 5,849,792; 5,889,052; 6,011,062 and 6,235,781

* A washout period of 4 weeks was followed by 2 weeks of TRAVATAN® Solution (n=16) or latanoprost monotherapy (n=18). At day 14, the final dose was administered at 8 pm and IOP measurements were taken. Baseline values for the two treatment groups were not significantly different. The standard deviations for the TRAVATAN® group were 3.9 mm Hg (12 hours), 2.9 mm Hg (16 hours), 3.2 mm Hg (20 hours), and 2.1 mm Hg (24 hours). For the latanoprost group, the standard deviations were 3.8 mm Hg (12 hours), 3.0 mm Hg (16 hours), 3.2 mm Hg (20 hours), and 3.1 mm Hg (24 hours). The difference between the two groups at 24 hours post dose was statistically significant (p=0.0117).

Reference 1. Dubiner HB, Sircy MD, Landry T, et al. Comparison of the diurnal ocular hypotensive efficacy of travoprost and latanoprost over a 44-hour period in patients with elevated intraocular pressure. Clin Ther. 2004;26:84-91.

Alcon®

Asian Journal of
OPHTHALMOLOGY

Volume 9 Number 2 April 2007

SEAGIG
South East Asia Glaucoma Interest Group

Asian Journal of OPHTHALMOLOGY is the official peer-reviewed journal of the South East Asia Glaucoma Interest Group (SEAGIG) and is indexed in EMBASE/Excerpta Medica. The website of *Asian Journal of OPHTHALMOLOGY* and SEAGIG membership details can be found at **www.seagig.org**.

As new technologies and therapeutic interventions are continually being developed, ophthalmology has become a field of rapid change, particularly in the Asia-Pacific region, where disease patterns and health care delivery differ greatly from those seen in the West. *Asian Journal of OPHTHALMOLOGY* was established in 1998 and became the official journal of SEAGIG in 2003, with the aim of disseminating information relevant to ophthalmology and glaucoma throughout Asia and to interested groups worldwide. The objectives of *Asian Journal of OPHTHALMOLOGY* are as follows:

- to provide a platform for the publication of information with a focus on ophthalmology in Asia
- to disseminate information that will improve the care of patients with all types of ophthalmological disorders, with a special focus on glaucoma
- to increase the understanding of such disorders through reporting of educational activities
- to publish the results of research programmes to expand knowledge about the causes, prevention, and treatment of ophthalmological disorders
- to work closely with Asian and international researchers to achieve these aims
- to provide a forum for young and relatively inexperienced researchers to present their research results as Original Articles via an international platform
- to maintain and promote relationships with any organisation with similar goals.

Although the focus of *Asian Journal of OPHTHALMOLOGY* is on glaucoma, other topics relevant to the region will not be ignored, and submissions on all aspects of ophthalmology are welcome.

SEAGIG is grateful to the following sponsors:
Platinum: Alcon Pfizer *Silver:* ALLERGAN

Scientific Communications

ISSN 1560-2133

Editorial Office
Scientific Communications
International Limited
Suite C, 10/F, Wo On Building
10 Wo On Lane, Central, Hong Kong
Tel: (852) 2868 9171
Fax: (852) 2868 9269
E-mail: editor@seagig.org

Manuscript Submissions
Information for Authors is available at the SEAGIG website (www.seagig.org), where manuscripts can be submitted online. Manuscripts can also be e-mailed to Kayoko Welsh at: manuscripts@seagig.org

Subscriptions
Please visit www.seagig.org to subscribe online. For queries and address changes, e-mail: idachan@scientific-com.com

Advertising Enquiries
To advertise in the Journal or SEAGIG website, or to become a SEAGIG sponsor, please visit www.seagig.org to access the Media Kit. Please e-mail any advertising/sponsorship queries to: info@seagig.org

Back Issues and Reprints
A limited number of back issues are available from the publisher. Reprints in large quantities for commercial or academic use may be purchased from the publisher. For information and prices, e-mail: idachan@scientific-com.com

Asian Journal of OPHTHALMOLOGY is distributed to 3500 ophthalmologists throughout Asia, with bonus distribution of up to 4000 copies at international conferences. The Chinese edition of *Asian Journal of OPHTHALMOLOGY*, *Yazhou Yanke Zazhi*, is distributed to over 5000 ophthalmologists in Mainland China.

SEAGIG is a member of the International Federation of Ophthalmological Societies.

LUMIGAN® (bimatoprost ophthalmic solution) 0.03% is indicated for the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension who are intolerant of other IOP-lowering medications or insufficiently responsive (failed to achieve target IOP determined after multiple measurements over time) to another IOP-lowering medication.

IMPORTANT SAFETY INFORMATION

LUMIGAN® (bimatoprost ophthalmic solution) 0.03% has been reported to cause changes to pigmented tissues. These reports include increased pigmentation and growth of eyelashes and increased pigmentation of the iris and periorbital tissue (eyelid). These changes may be permanent.

The most frequently reported adverse events occurring in approximately 15% to 45% of patients dosed once daily, in descending order of incidence, were conjunctival hyperemia, growth of eyelashes, and ocular pruritus.

See LUMIGAN® Prescribing Information.

Visit us at www.lumigan.com

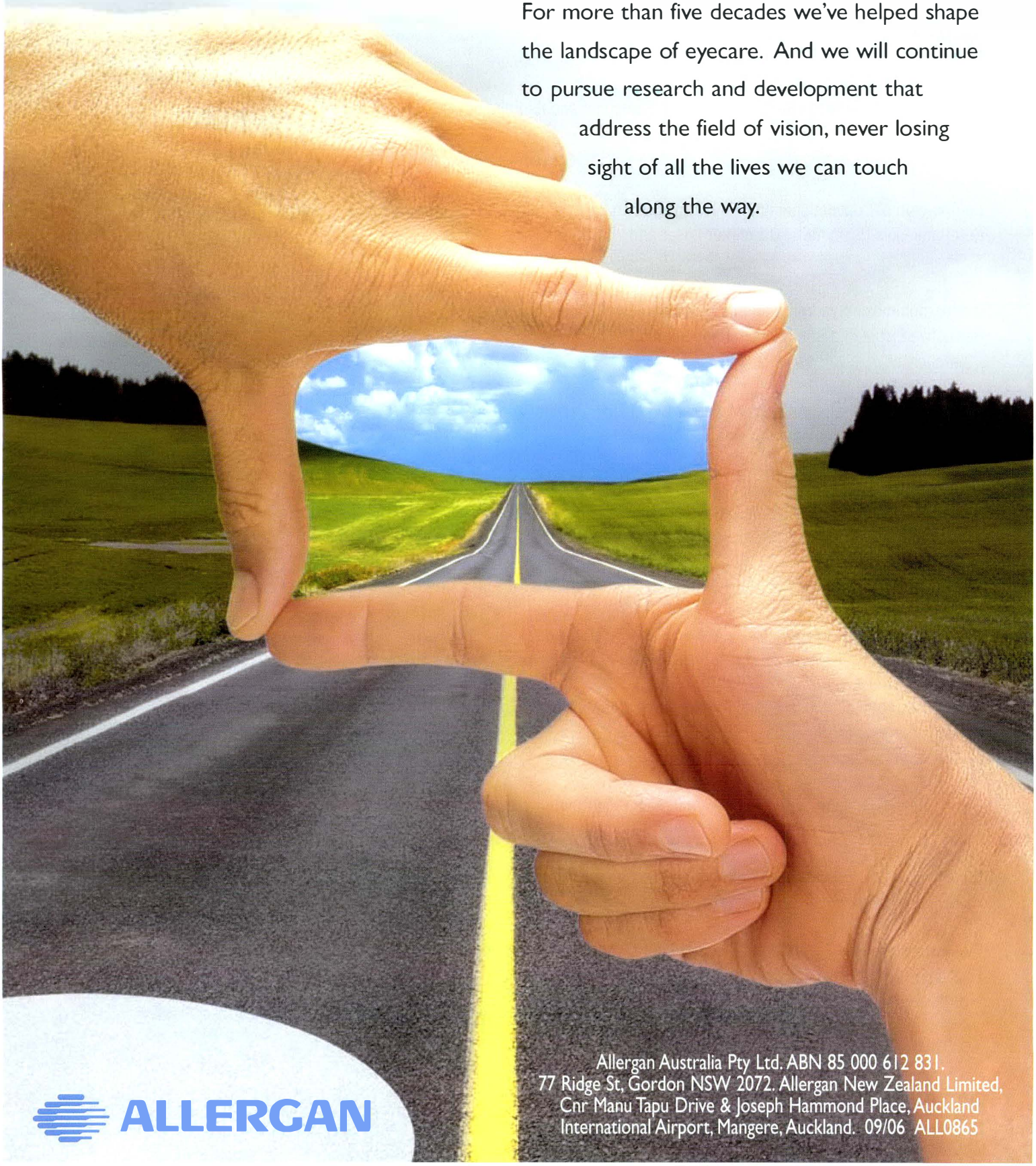
LUMIGAN®
(bimatoprost ophthalmic solution) 0.03%

Asian Journal of
OPHTHALMOLOGY
Volume 9 Number 2 April 2007

Table of Contents

No limits in sight

Allergan Eyecare is focused on the future, and on the unlimited possibilities in sight. For more than five decades we've helped shape the landscape of eyecare. And we will continue to pursue research and development that address the field of vision, never losing sight of all the lives we can touch along the way.



ALLERGAN

Allergan Australia Pty Ltd. ABN 85 000 612 831.
77 Ridge St, Gordon NSW 2072. Allergan New Zealand Limited,
Cnr Manu Tapu Drive & Joseph Hammond Place, Auckland
International Airport, Mangere, Auckland. 09/06 ALL0865

Initiative for Management, Awareness and Glaucoma Education: Modules 3 and 4

SEAGIG-IMAGE Project Working Group

The South East Asia Glaucoma Interest Group (SEAGIG) is pleased to announce the release of the second 2 modules of the educational resource from the Initiative for Management, Awareness and Glaucoma Education (IMAGE) project. Intended for use by ophthalmologists for their own educational advancement, as well as to facilitate educational programmes, the slides have been prepared by SEAGIG/IMAGE members to be clinically relevant to glaucoma care in the region and to have educational value relevant to the region.

The *Optic Disc Assessment/RNFL Overview* module highlights the key role that optic nerve examination plays in the diagnosis and follow-up of patients with glaucoma. This module outlines a systematic method of evaluating the optic disc and documenting glaucoma-related findings as well as disease progression.

The *Automated Perimetry* module is intended to act as a practical guide to automated perimetry and its role in the diagnosis of glaucoma. Sample printouts are provided throughout the module to show clinicians how to interpret perimetry results in a systematic manner.

Optic Disc Assessment/RNFL Overview

Recognising the characteristic features of glaucomatous optic neuropathy is a critical component in identifying and caring for patients with glaucoma. The 5 rules for assessing the optic disc and RNFL in glaucoma will be introduced, followed by separate sections focused on detecting glaucoma and disease progression. With practice, the clinician can perceive glaucomatous changes easily and accurately using the information provided in these slides. Sample photographs are included for the purposes of discussion and testing participants' skills.

At the end of the presentation, participating clinicians should be able to:

- list the 5 rules for assessing the optic nerve in glaucoma (Figure 1)
- use the 5 rules in a systematic, confident manner to identify the presence of glaucomatous changes in the optic nerve
- diagnose glaucoma and describe its progression in patients undergoing ophthalmological examination
- distinguish between photographs of normal and glaucomatous or pathological optic nerves (Figure 2)
- accurately identify the presence of glaucoma and describe any characteristic signs in the photographs in sections IV and V (Figure 3).

Correspondence: Dr Prin RojanaPongpun, Department of Ophthalmology, Chulalongkorn University, Bangkok, Thailand.
Fax: (662) 256 4425;
E-mail: rprin@chula.ac.th

Figure 1.

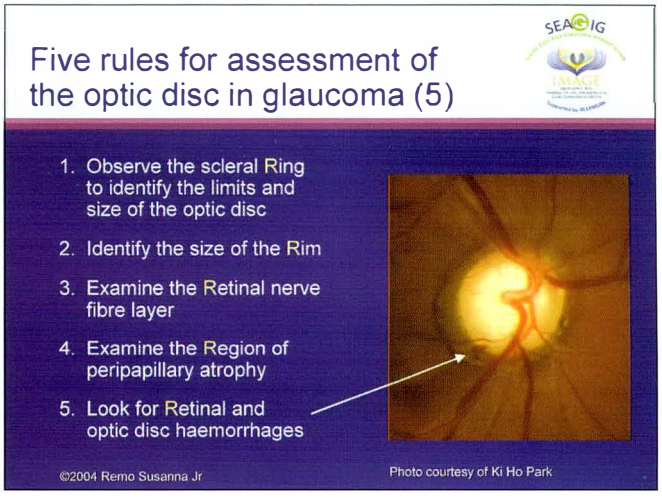
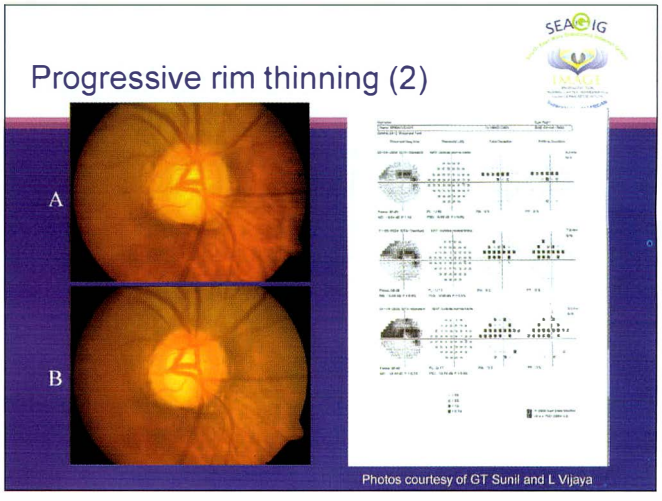


Figure 2.



Automated Perimetry

Automated perimetry is the gold standard for diagnosis and

Figure 3.

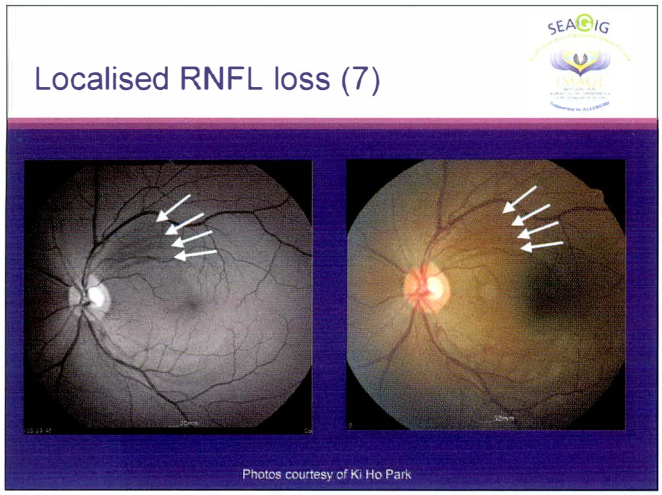


Figure 4.

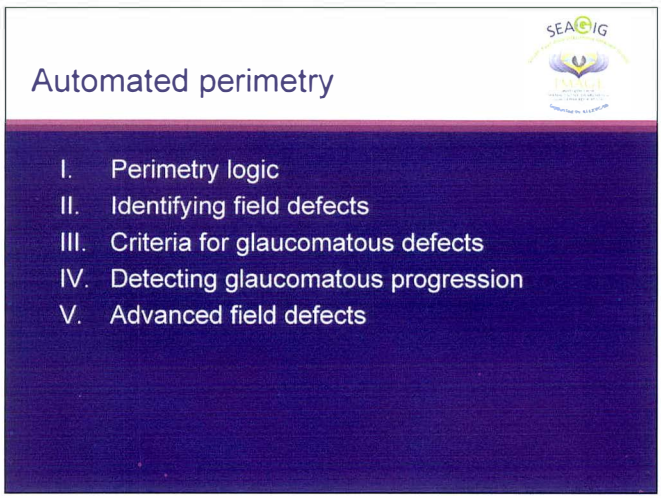


Figure 5.

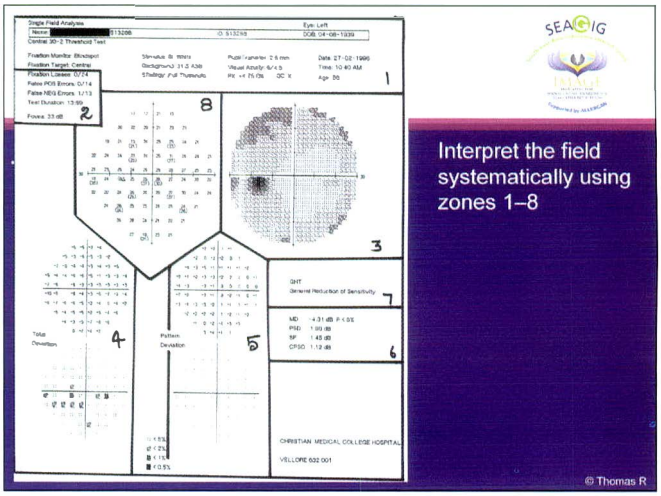
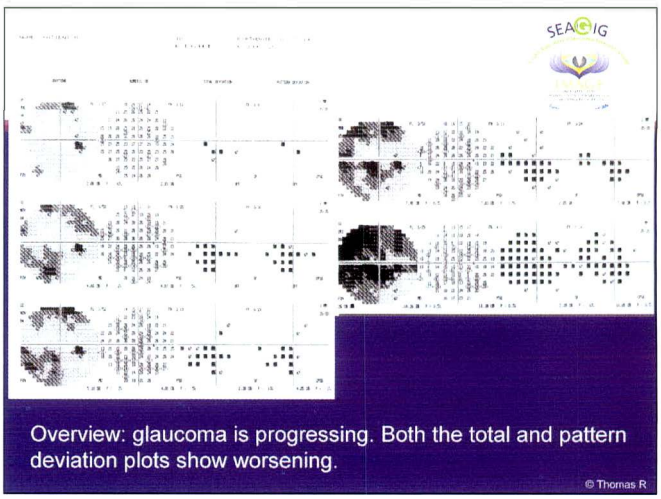


Figure 6.



management of glaucoma. A careful appraisal of an automated perimetry printout will enable the practitioner to identify a visual field defect, determine whether the defect is due to glaucoma, and establish whether the lesion is progressing. However, interpretation requires both an understanding of the principles involved and practice.

After an introduction to the basics of automated perimetry (Figure 4), this module covers 3 topics of clinical importance:

- how to interpret the visual field systematically (Figure 5)
- how to determine whether the defect is due to glaucoma
- how to detect glaucomatous change (Figure 6).

Lastly, this module covers advanced field defects, which may require different perimetric strategies than less advanced defects.

Sample printouts are provided throughout the module to help familiarise the clinician with how to interpret perimetry results in a systematic manner.

Acknowledgement

With gratitude to the members of the SEAGIG-IMAGE Project Working Group: Dr Manuel Agulto, The Philippines; Prof Paul Chew, Singapore; Dr John Chua, Hong Kong; Dr Ataya Euswas, Thailand; Dr Seng Kheong Fang, Malaysia; Assoc Prof Ivan Goldberg, Australia; Dr Paul Healey, Australia; Dr Edgar Leuenberger, The Philippines; Dr Da-Wen Lu, Taiwan; Dr Vinay Nangia, India; Assoc Prof Chan Kee Park, Korea; Assoc Prof Ki Ho Park, Korea; Assoc Prof Julian Rait, Australia; Dr Prin RojanaPongpun, Thailand; Prof Ravi Thomas, India; Dr Lingam Vijaya, India; Dr Ningli Wang, China. With grateful thanks to Dr RN Weinreb, Dr FA Medeiros, and Dr R Susanna for provision of the slides for the *Optic Disc Assessment/RNFL Overview* module.

Reference

South East Asia Glaucoma Interest Group. Asia Pacific Glaucoma Guidelines. Singapore: SEAGIG, 2003-2004. Available at: www.seagig.org/pdf/APGGuidelinesNMview.pdf.

Vision-related Quality of Life of Patients with Glaucoma and its Relationship with Visual Function in China

Yu Zhang, Chun Zhang, Wei Wang
Peking University Eye Center, Peking University Third Hospital, Beijing, China

Objective: *To investigate vision-related quality of life of Chinese patients with glaucoma and to evaluate the relationship between subjective vision-related quality of life and visual function.*
Methods: *102 Chinese patients with glaucoma were enrolled and divided into 2 groups: group A had daily life visual acuity ≥0.8 (70 patients) and group B had daily life visual acuity <0.8 (32 patients). According to the severity of visual field impairment, the patients in group A were divided into 2 groups: group A_1 (mean deviation, <10; 49 patients) and group A_2 (mean deviation, ≥10; 21 patients). Thirty patients were enrolled as a control group. All patients completed a questionnaire and received daily life visual acuity and visual field examination. Vision-related quality of life score and binocular mean deviation were calculated and analysed by Pearson relevance analysis and single factor analysis of variance.*
Results: *There were significant differences in the total scores for vision-related quality of life, binocular mean deviation, daily life visual acuity and self-evaluation scores between the patients with glaucoma and the control group ($p < 0.001$). There was a significant correlation between the total scores for vision-related quality of life and binocular mean deviation, daily life visual acuity, and self-evaluation scores in group A, group B, and the control group. There was no significant difference in age and daily life visual acuity between group A_1, group A_2, and the control group, but there was a significant difference in the total score of vision-related quality of life between group A and the control group ($p < 0.001$). Compared with the control group, the average score for dark adaptation, and reading and writing in group A_1 was significantly decreased ($p < 0.05$).*
Conclusions: *There is significant correlation between the score for vision-related quality of life and visual field defects of both eyes, which can reflect the severity of glaucoma. The impairment of dark adaptation, and reading and writing capacity is most significant in the earlier stage of glaucoma in the Chinese population.*

Key words: *Glaucoma, Quality of Life, Questionnaires, Vision*

Asian J Ophthalmol. 2007;9:59-63

Introduction

Glaucoma is one of the commonest causes of blindness worldwide. As the condition worsens, vision-related quality of life (VRQL) decreases. In 1996, Zimmerman et al began to divert the focus of treatment from clinical manifestations to patients' quality of life.[1,2] Outcome assessment has become increasingly important as a critical measure for treatment and management of medical conditions. Zimmerman et al[1,2] and Lee[3] have highlighted the need for patient-centered care in glaucoma and placed emphasis on individualised treatment. Many clinicians have used vision-specific instruments to establish the relationship between VRQL and clinical indicators for patients with glaucoma;[4-13] these include Activities of Daily Vision Scores, National Eye Institute Visual Functioning Questionnaire, and the Visual Functioning-14 Questionnaire.[14] Patients with glaucoma have low scores, indicating less functional vision-specific status in patients with glaucoma when compared with normal controls. Viswanathan et al noted a significant relationship between perceived visual disability and the severity of binocular field loss in patients with early and moderate glaucomatous visual field loss.[15] Nelson et al designed a new questionnaire, the Glaucoma Quality of Life-15 (GQL-15), which had better correlativity with multiple clinical parameters.[16] Two surveys addressed the issue of symptoms of glaucoma and its

Correspondence: Dr Chun Zhang, Peking University Eye Center, Peking University Third Hospital, 49 North Garden Road, Haidian District, Beijing, 100083, China.
Tel: (86 10) 6201 7691/6573; Fax: (86 10) 8208 9951;
E-mail: zhangc1@163.com

treatment: the Comparison for the Ophthalmic Medications for Tolerability[17] and the Glaucoma Symptom Scale.[18] Both surveys assess the presence of ocular, non-visual, and visual symptoms often associated with disease progression and glaucoma treatment. Generic health-related quality of life measures have also been used to investigate quality of life in glaucoma. The Medical Outcomes Study Short Form (MOS-SF 36 and MOS-SF 24) questionnaires[19] have been used in a number of studies that found lower scores, indicating a decrease in well being and functional status in patients with glaucoma.[4-6,9,13,20] Since there are differences in living environment, lifestyles, and management of glaucoma throughout the world, it was necessary to design a quality of life questionnaire suitable for patients with glaucoma in China to guide the management of the disease. This study investigated the VRQL of Chinese patients with glaucoma and evaluated the relationship between subjective VRQL and visual function.

Methods

Patients

102 patients with a confirmed diagnosis of glaucoma who attended Peking University Eye Center, Beijing, China, from March 2003 to July 2003, were enrolled into the study. Fifty nine patients had primary angle closure glaucoma, 32 had primary open angle glaucoma, 6 had secondary glaucoma, and 5 had normal tension glaucoma. All patients had visual field defects in both eyes (mean deviation [MD], >2). Anyone with systemic diseases such as heart disease, uncontrolled hypertension, cerebrovascular disease, mental disorders, or other eye diseases affecting visual function such as cataract or age-related macular degeneration were excluded. All enrolled patients had normal comprehension, were willing to complete the investigation, and had no surgical history within 3 months of starting the study. Thirty age-matched participants with no history of glaucoma were enrolled as controls. All control participants met the above criteria with normal visual field indices (MD, <2; loss of variance [LV], <6) and daily life visual acuity (DLVA, distant vision of both eyes under daily life conditions) >0.8. According to the DLVA, all patients were divided into 2 groups: group A (DLVA, ≥0.8; 70 patients) and group B (DLVA, <0.8; 32 patients). According to the severity of visual field impairment, the patients in group A were divided into subgroups of group A_1 (MD, <10; 49 patients) and group A_2 (MD, ≥10; 21 patients).

Questionnaire and Scoring

The questionnaire was administrated to all patients by the same interviewer. If the participants could not read the questionnaire, the interviewer read the questionnaire to them. The questionnaire was designed in 2 parts: part I related to VRQL questions (22 items) and part II consisted of self-evaluation scores (3 items). Part I consisted of 6 aspects relating to daily life: reading and writing, walking, dark adaptation, housework, driving, and outdoor mobility (Table 1). There were 6 options for each question, based on the difficulty of accomplishment: A "have no difficulty" scored 4; B "have a little difficulty" scored 3; C "difficult" scored 2; D "very difficult" scored 1; E "unable due to low visual acuity" scored 0; and F "have not performed or feel difficult due to other reasons" was not included in the statistical study. The average score for each question was multiplied by 25 to obtain the total VRQL score in a 100-mark system, and the respective average score of each of the 6 life aspects was calculated. Part II included a self-rated visual acuity score, subjective brightness score, and subjective visual field score. Scoring scales of 0 to 10 were used for each question: 0 indicated the worst condition and 10 indicated the best condition. The average score of the 3 questions was calculated.

Eye Examination

All participants underwent a comprehensive ophthalmic evaluation, including review of medical history, binocular daily life, and monocular best-corrected visual acuity testing with the International Standard Eye Chart, and 30° visual field with the Octopus 101 perimeter (tG2 program; HAAG STREIT AG, Koeniz-Berne, Switzerland). The reliability factor was required to be <15% and the visual field indices (mean sensitivity [MS]; MD; LV) of both eyes were obtained. MD values for both eyes were obtained following the equation $MD_{ou} = (MD^2_{od} + MD^2_{os})^{1/2}$, which was modified from the calculation method in Nelson-Quigg et al.[21]

Table 1. Vision-related quality of life questions of 6 aspects of daily life.

Reading and writing	Walking	Dark adaptation	Housework	Driving	Outdoor mobility
Reading street signs	Recognising people on the road	Walking in the dark	Washing clothes or cooking	Riding a bicycle	Meeting people in their homes or restaurants
Reading newspaper	Crossing the road	Going from light to dark room	Finding something on a crowded shelf	Driving in the daytime	Taking part in sports
Playing card games	Bumping into objects		Sewing	Driving at night	Shopping
Watching television	Walking slowly				
Reading labels on eye bottles					
Filling out forms					

Table 2. Vision-related quality of life, mean deviation, visual acuity, and self-evaluation scores for patients with glaucoma and controls.

	Mean (SD)			
	Patients with glaucoma (n = 102)	Controls (n = 30)	t	p Value
Age (years)	65.03 (11.28)	62.67 (7.83)	1.07	0.286
Vision-related quality of life	89.58 (12.28)	98.94 (1.98)	-7.38	0.000
Binocular mean deviation	9.46 (10.41)	0.37 (0.92)	8.70	0.000
Binocular visual acuity	0.80 (0.22)	0.97 (0.08)	-5.81	0.000
Self-evaluation score	7.12 (1.45)	8.92 (0.93)	-10.45	0.000

Table 3. Correlation between vision-related quality of life score and mean deviation, visual acuity, and self-evaluation in group A, group B, and controls.

	Vision-related quality of life					
	Group A (n = 70)		Group B (n = 32)		Controls (n = 30)	
	r	p Value	r	p Value	r	p Value
Binocular mean deviation	-0.257	0.031	-0.463	0.008	-0.491	0.006
Binocular visual acuity	0.293	0.014	0.439	0.012	0.396	0.031
Self-evaluation	0.646	<0.001	0.838	<0.001	0.679	<0.001

Statistical Analysis

The Statistical Package for the Social Sciences 11.0 software was used to conduct Pearson relevance analysis, independent sample *t* test, and single factor analysis of variance. Statistical significance was inferred at a value of $p < 0.05$.

Results

102 Chinese patients with glaucoma (35 men and 67 women) and 30 controls were enrolled in the study. There were significant differences in the total score for VRQL, binocular MD, and DLVA and self-evaluation score between the 102 patients and the control group (Table 2). There was a significant correlation between the total score for VRQL and binocular MD, DLVA, and self-evaluation in group A, group B, and the control group (Table 3).

There were no inter-group differences in age and visual acuity between group A_1, group A_2, and the control group, but there was a significant inter-group difference for the total score for VRQL (Table 4). The mean scores for group A_1, group A_2, and the control group are shown in Table 5. There were significant inter-group differences for dark adaptation, and reading and writing between group A_1 and the control group.

Discussion

In this study, a questionnaire was used to investigate the VRQL of patients with glaucoma and to evaluate the relationship between subjective VRQL and objective visual function examination. There was a significant correlation between the VRQL score and visual field defects, which may reflect the severity of glaucoma. The impairment of dark adaptation and reading and writing capacity was most significant in the early stage of glaucoma (MD, <10 dB).

When the influence of systemic diseases and age had been excluded, there was a significant difference in the VRQL score,

Table 4. Age, visual acuity, and vision-related quality of life score in group A_1, group A_2, and controls.

	Mean (SD)			F	p Value
	Group A_1 (n = 49)	Group A_2 (n = 21)	Controls (n = 30)		
Age (years)	62.90 (12.47)	62.38 (10.88)	62.67 (7.83)	0.017	0.983
Binocular visual acuity	0.94 (0.13)	0.90 (0.12)	0.96 (0.09)	2.137	0.124
Vision-related quality of life score	94.28 (7.75)	86.95 (14.18)	98.93 (1.98)	12.27	0.000

Table 5. Mean scores for the 6 aspects of vision-related quality of life for group A_1, group A_2, and controls.

	Mean (SD)			F	p Value
	Group A_1 (n = 49)	Group A_2 (n = 21)	Controls (n = 30)		
Reading and writing*	3.85 (0.29)	3.49 (0.60)	3.98 (0.75)	14.19	0.000
Walking	3.72 (0.49)	3.46 (0.65)	3.90 (0.18)	5.43	0.006
Dark adaptation*	3.57 (0.47)	3.26 (0.66)	3.93 (0.17)	13.83	0.000
Housework	3.73 (0.39)	3.42 (0.71)	3.99 (0.06)	11.08	0.000
Driving	3.43 (1.20)	3.36 (1.45)	4.00 (0.00)	2.11	0.131
Outdoor mobility	3.84 (0.33)	3.69 (0.57)	3.95 (0.13)	3.46	0.036

* $p < 0.05$ group A_1 versus controls.

binocular MD, and DLVA and the self-evaluation score between patients with glaucoma and the control group, indicating that VRQL and objective visual function indices of patients with glaucoma are decreased.

Nelson et al enrolled patients with comparatively good visual acuity (mean, 6/9 to 6/4; average, 6/6) to eliminate the influence of visual acuity on the scores.[16] As a result, the applicability of the questionnaire was impaired. To avoid this problem, the range of visual acuities of patients in this study was increased. Based on the average visual acuity of 0.8, the patients were divided into 2 groups. In group A, the correlation coefficient of VRQL score and binocular MD was -0.257, which was lower than that of the GQL-15[16] (r = -0.6) and VF-14[5] (r = -0.58) in other studies. In group B, the correlation coefficient of VRQL score and binocular MD was -0.463, which was similar to the results published by Ross et al[22] and Mills and Drance,[23] indicating that VRQL had better correlativity with visual field in patients with glaucoma with comparatively low visual acuity.

The self-evaluation score verified the reliability of the VRQL answers. The questions in the self evaluation were consistent with some questions of the VQL, indicating the comprehension of the patients and the reliability of the answers. The total VRQL score had significant correlation with self-evaluation score in group A, group B, and the control group, indicating that the answers had good conformability and the investigation results were reliable.

To eliminate the influence of DLVA on the scores, group A was further subdivided into group A_1 and group A_2, based on binocular MD, and compared with the control group. Group A_1, group A_2, and the control group had no significant inter-group differences for age and visual acuity, but there was significant inter-group difference for the total VRQL score. Therefore, the total VRQL score reflected the severity of glaucoma to some extent. This agreed with the significant difference of GQL-15 score between the control group and the patients with impaired visual fields (mild, moderate, serious) in the study by Parrish,[9] but the classification was based on morphological visual field changes (mild: unilateral visual field defect <50%; moderate: unilateral visual field defect >50% or bilateral visual field defects <50%; serious: bilateral visual field defects >50%).

According to the VRQL 6 classification statistics, there were significant differences in reading and writing, walking, dark adaptation, housework, and outdoor mobility between healthy Chinese individuals, those with mild visual field impairment, and those with serious visual field impairment, which is similar to results for western populations.[16,24] Among the Chinese patients with glaucoma, dark adaptation, and reading and writing capacities were the first factors to become impaired. This result is also similar to that of western populations.[16] Based on this result, warning Chinese patients with different stages of glaucoma about the difficulties they may face in daily life will enable them to take corresponding measures to protect themselves. For example, as the dark adaptation capacity may be impaired in the early stages of glaucoma, patients may change their indoor lighting conditions accordingly.

References

1. Zimmerman TJ, Karunaratne N, Fechtner RD. Glaucoma: outcomeology (part I). J Glaucoma. 1996;5:151.
2. Zimmerman TJ, Karunaratne N, Fechtner RD. Glaucoma: outcomeology (Part II). J Glaucoma. 1996;5:152-5.
3. Lee P. Outcomes and endpoints in glaucoma. J Glaucoma. 1996; 5:295-7.
4. Gutierrez P, Wilson MR, Johnson C, et al. Influence of glaucomatous visual field loss on health-related quality of life. Arch Ophthalmol. 1997;115:777-84.
5. Parrish R 2nd, Gedde SJ, Scott I, et al. Visual function and quality of life among patients with glaucoma. Arch Ophthalmol. 1997;115: 1447-55.
6. Sherwood M, Garcia-Siekavizza A, Meltzer M, et al. Glaucoma's impact on quality of life and its relation to clinical indicators. Ophthalmology. 1998;105:561-6.
7. Magacho L, Lima FE, Nery AC, et al. Quality of life in glaucoma patients: regression analysis and correlation with possible modifiers. Ophthalmic Epidemiol. 2004;11:263-70.
8. Jampel HD, Schwartz A, Pollack I, et al. Glaucoma patients' assessment of their visual function and quality of life. J Glaucoma. 2002;11:154-63.
9. Parrish RK 2nd. Visual impairment, visual functioning, and quality of life assessments in patients with glaucoma. Trans Am Ophthalmol Soc. 1996;94:919-1028.
10. Nah YS, Seong GJ, Kim CY. Visual function and quality of life in Korean patients with glaucoma. Korean J Ophthalmol. 2002;16: 70-4.
11. Jampel HD, Friedman DS, Quiqley H, et al. Correlation of the binocular visual field with patient assessment of vision. Invest Ophthalmol Vis Sci. 2002;43:1059-67.
12. Hyman LG, Komaroff E, Heijl A, et al. Early Manifest Glaucoma Trial Group. Treatment and vision-related quality of life in the early manifest glaucoma trial. Ophthalmology. 2005;112:1505-13.
13. Hirneiss C, Neubauer AS, Welge-Lussen U, et al. [Measuring patient's quality of life in ophthalmology.] Ophthalmologe. 2003; 100:1091-7.
14. Steinberg E, Tielsch J, Schein O, et al. The VF-14. An index of functional impairment in patients with cataract. Arch Ophthalmol. 1994; 112:630-8.
15. Viswanathan A, McNaught A, Poinoosawmy D, et al. Severity and stability of glaucoma: patient perception compared with objective measurement. Arch Ophthalmol. 1999;117:450-4.
16. Nelson P, Aspinall P, Papasouliotis O, et al. Quality of life in glaucoma and its relationship with visual function. J Glaucoma. 2003; 12:139-50.
17. Barber B, Strahlman E, Laibovitz R, et al. Validation of a questionnaire for comparing the tolerability of ophthalmic medications. Ophthalmology. 1997;104:334-42.
18. Lee B, Gutierrez P, Gordon M, et al. The Glaucoma Symptom Scale: a brief index of glaucoma-specific symptoms. Arch Ophthalmol. 1998;116:861-6.
19. Wilson M, Coleman A, Yu F, et al. Functional status and well being

in patients with glaucoma as measured by the Medical Outcomes Study Short Form-36 Questionnaire. Ophthalmology. 1998;105: 2112-6.
20. Cypel MC, Kasahara N, Atique D, et al. Quality of life in patients with glaucoma who live in a developing country. Int Ophthalmol. 2004;25:267-72.
21. Nelson-Quigg J, Cello K, Johnson CA. Predicting binocular visual field sensitivity from monocular visual field results. Invest Ophthalmol Vis Sci. 2000;41:2212-21.
22. Ross J, Bron A, Clarke DD. Contrast sensitivity and visual disability in chronic-simple glaucoma. Br J Ophthalmol. 1984;68:821-7.
23. Mills R, Drance S. Esterman disability rating in severe glaucoma. Ophthalmology. 1986;3:371-8.
24. Nelson P, Aspinall P, Brien CO. Patients' perception of visual impairment in glaucoma: a pilot study. Br J Ophthalmol. 1999;83: 546-52.

Comparison of Conventional and Wavefront-guided Laser in Situ Keratomileusis Using MEL 70 Excimer Laser and WASCA Analyzer

Sabong Srivannaboon
Department of Ophthalmology, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand

Aim: *To compare the refractive outcome of laser in situ keratomileusis with and without wavefront-guided ablation.*
Methods: *Forty eyes of 20 patients with mild to moderate myopia were included in the study. Laser in situ keratomileusis was performed in each patient using a Hansatome microkeratome and a MEL 70 G-Scan Excimer Laser. In 10 patients (20 eyes) this was followed by wavefront aberration supported cornea ablation (group 1). The remaining 20 eyes did not receive this additional treatment (group 2). All patients were assessed preoperatively and 1 week, 1 month, and 6 months after laser in situ keratomileusis. Assessment included manifest refraction and visual acuity.*
Results: *Data collected preoperatively showed no statistically significant differences between the 2 groups. The mean preoperative refractive error (spherical equivalent) was -4.38 D (SD, 1.78 D) in group 1 and -5.31 D (SD, 1.92 D) in group 2. Group 1 showed significantly better refraction than group 2 at all follow-up time points ($p < 0.05$). Six months after laser in situ keratomileusis, refraction was within ±1 D of the intended value for 100% of patients in group 1 and 90% in group 2. A gain in visual acuity of 1 Snellen line was achieved in 30% of group 1 and 15% in group 2 and visual acuity was 20/40 or better in 100% and 90% of patients in groups 1 and 2, respectively.*
Conclusion: *The outcome of wavefront-guided laser in situ keratomileusis was superior to that of non-wavefront–guided laser in situ keratomileusis 6 months after treatment.*

Key words: *Astigmatism, Comparative study, Keratomileusis, laser in situ, Myopia, Refractive errors*

Asian J Ophthalmol. 2007;9:64-7

Introduction

Wavefront technology, which provides detailed information about the eye's optical system, is used by ophthalmologists throughout the world. Much research has been conducted to explore the outcome of wavefront-guided laser in situ keratomileusis (LASIK) during the past few years.[1-4] Some authors have discussed the possibility of achieving supernormal vision with wavefront-guided LASIK.[1,5] However, the visual benefit of wavefront-guided LASIK compared with conventional LASIK for people with myopia has not yet been established. This study was undertaken to compare the results of wavefront-guided LASIK with non-wavefront-guided LASIK.

Correspondence: Dr Sabong Srivannaboon, Department of Ophthalmology, Faculty of Medicine, Siriraj Hospital, Mahidol University, 2 Prannok Rd, Bangkoknoi, Bangkok 10700, Thailand.
Tel: (66 2) 419 8033; Fax: (66 2) 411 1906;
E-mail: sabong@pol.net

Methods

Twenty eligible patients who attended the Excimer Laser Clinic at the Department of Ophthalmology, Siriraj Hospital, Bangkok, Thailand, during January and February 2002 were included in the study. Preoperative evaluation for LASIK included routine slit-lamp biomicroscopy, indirect ophthalmoscopy, manifest and cycloplegic refraction, Goldmann tonometry, and Orbscan corneal topography for corneal curvature and corneal thickness. Wavefront-guided LASIK was randomly performed in both eyes of 10 patients (wavefront aberration supported cornea ablation [WASCA] group; group 1) and non-wavefront guided LASIK was performed in both eyes of the remaining 10 patients (non-WASCA group; group 2). A WASCA Analyzer (Carl Zeiss Meditec, Jena, Germany) was used to measure wavefront aberration in the eyes of patients in group 1 using a 6 mm analysis zone. Three measurements were performed with cycloplegic medication and the best measurement was

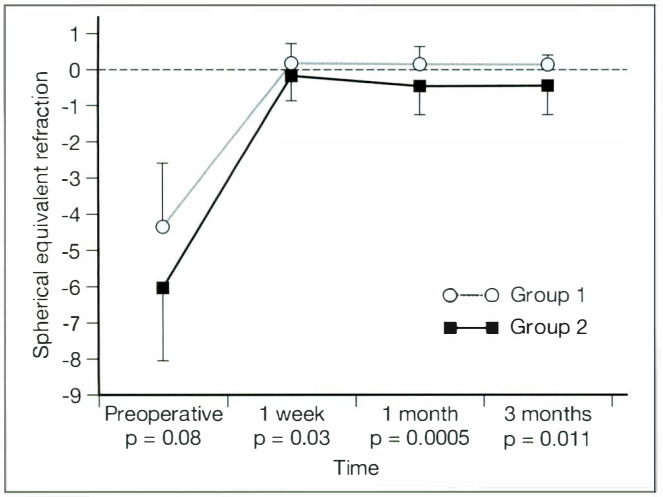
selected for the laser ablation based on the clarity of the Hartmann-Shack image.

All eyes underwent LASIK surgery according to the following conventional technique. Under topical anaesthesia, a Hansatome microkeratome (Bausch & Lomb, Rochester, USA) with an 8.5-mm ring size and 160-μm head was used to create a corneal flap. The flap was then lifted and the artificial limbus ring was placed to initiate the eye tracking system. The eye tracker was locked on the ring and fine adjustment for centration was made. After setting the dehydration time to 45 seconds, the laser ablation was performed using a MEL 70 G-Scan Excimer Laser (Carl Zeiss Meditec, Jena, Germany). Conventional laser ablation with direct setting of manifest refraction was performed for both groups. Additional wavefront-guided ablation was then performed for group 1 only. For all patients, the corneal flap was replaced and the eye was irrigated to clean the flap. Postoperative antibiotic eye drops and non-steroidal anti-inflammatory eye drops were administered. Each patient was examined 1 day, 1 week, 1 month, and 6 months postoperatively. Manifest refraction, uncorrected visual acuity (UCVA), and best corrected visual acuity (BCVA) were recorded. Statistical analysis of between-group differences in refraction at various time points was performed using the paired *t* test. Microsoft Excel 2002 software was used for this purpose. A p value of <0.05 was considered significant.

Results

The mean age of patients in group 1 was 34.8 years (SD, 8.7 years; range, 23 to 46 years) compared with 33.0 years (SD, 8.6 years; range,17 to 49 years) for patients in group 2. The mean preoperative manifest refraction (spherical equivalent) was -5.67 D (SD, 1.78 D; range, -1.50 to -8.60 D) for group 1 and -5.31 (SD, 1.92 D; range, -2.00 to -10.60 D) for group 2 ($p = 0.08$).

Figure 1. Changes in refraction following laser in situ keratomileusis.



Six months after surgery, the mean manifest refraction (spherical equivalent) was +0.10 D (SD, 0.19 D; range, -0.25 to +0.50 D) for eyes in group 1 and -0.40 D (SD, 0.57 D; range, -1.00 to +0.50 D) for eyes in group 2. The change in spherical equivalent refraction over time is shown in Figure 1. Manifest refraction was significantly lower in group 1 than in group 2 at 1 week, 1 month, and 6 months after surgery.

A plot of intended correction versus achieved correction at 6 months indicated good predictability of up to -9.00 D ($R^2 = 0.92$) in group 1 and the achieved correction for all eyes lay within ± 1.00 D of the intended value (Figure 2). Figure 3 shows that predictability was poorer for group 2 ($R^2 = 0.85$), in which only 80% of values achieved lay within ±1.00 D of the intended value. Also, there was a tendency towards slight undercorrection in eyes with high myopia. Postoperative defocus equivalent refraction

Figure 2. Intended versus achieved correction in group 1.

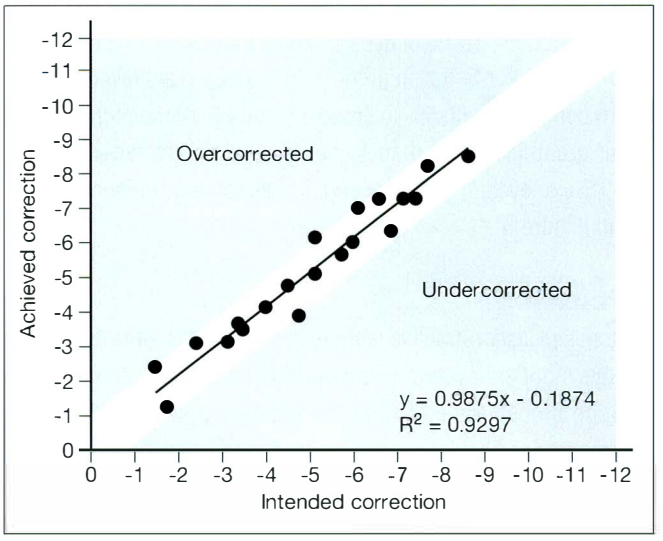


Figure 3. Intended versus achieved correction in group 2.

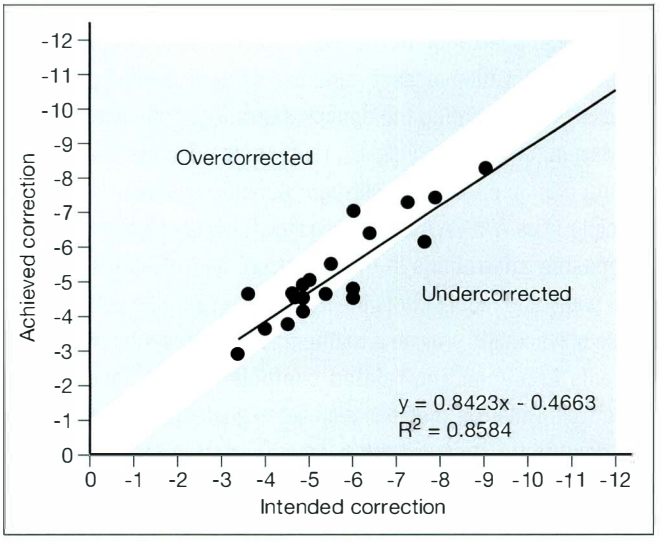


Figure 4. Postoperative defocus equivalent refraction.

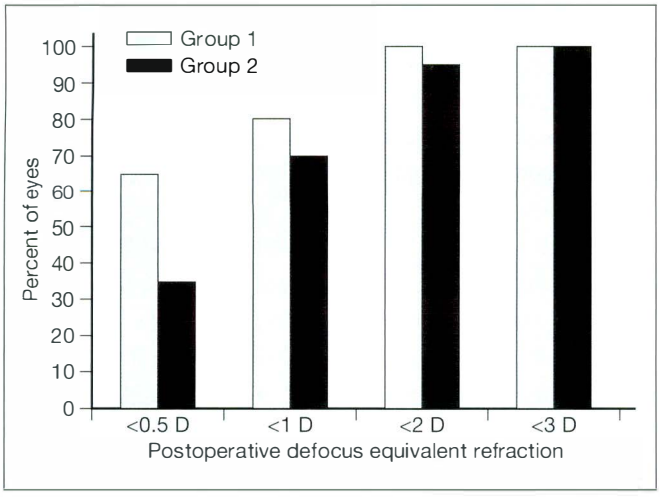
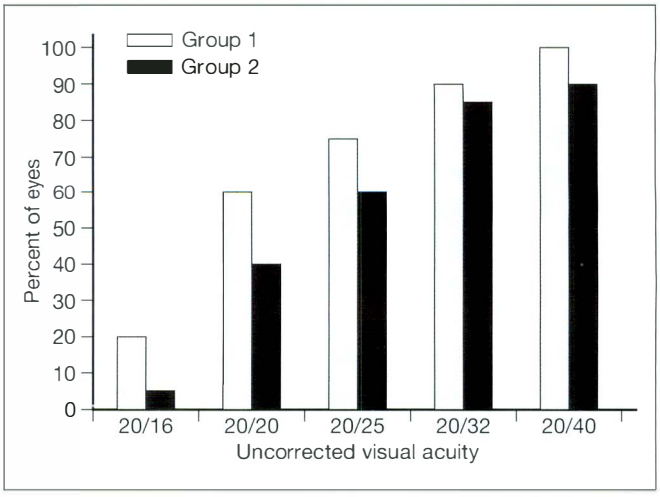


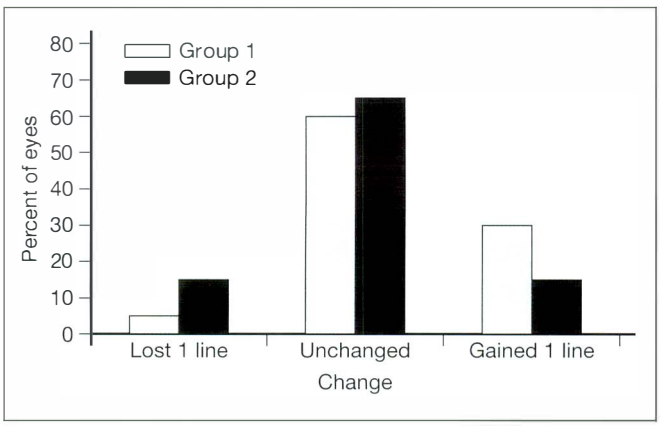
Figure 5. Cumulative uncorrected visual acuity.



was <0.50 D in 65% of eyes in group 1 and 35% of eyes in group 2 (Figure 4).

At 6 months, 100% of eyes in group 1 and 90% in group 2 had UCVA of 20/40 or better. In group 1, 20% of eyes achieved UCVA of 20/16 compared with 5% in group 2 (Figure 5). None of the eyes in either group lost more than 1 line of visual acuity, whereas 30% and 15% of eyes in groups 1 and 2, respectively, gained 1 line of vision (Figure 6).

Figure 6. Change in best-corrected visual acuity at 6 months.



Discussion

Customised laser refractive surgery is surgery that aims to improve the eye's optical system using various parameters to guide the ablation procedure, including refractive errors, corneal surface information, and ocular aberration. There are 2 types of customised laser refractive surgery. The first is corneal topography–guided ablation, which uses preoperative corneal topography to determine an ablation profile for the laser. The second is wavefront-guided ablation, in which the laser ablation profile is determined by the total optical aberration of the eye. Wavefront-guided ablation is the latest innovation in laser refractive surgery. Several principles are used for measuring the optical aberration of the eye, such as the Hartmann-Shack principle,[6] Tscherning principle,[7] single ray-tracing principle,[8] and the slit-light bundles-scanning skiascopy principle.[9] The WASCA Analyzer uses the Hartmann-Shack principle to measure aberrations in the wavefront as it deviates from an ideal plane and reconstructs the modal using Zernike polynomials. These polynomials provide a mathematical representation of a set of basis functions and related coefficients that describe the wavefront. The laser profile is then set to guide the laser to correct the deviated wavefront. With advances in laser technology, surgeons are now able to treat a wide range of refractive disorders such as refractive error with or without optical aberration.

In this study, wavefront-guided LASIK produced a significantly better refractive outcome than non-wavefront-guided LASIK at all follow-up time points during the 6-month study period. Both the mean spherical equivalent refraction and the standard deviation were lower in group 1 and 100% of the eyes in this group were within ±1 D of the intended value. Moreover, a higher percentage of eyes in this group achieved low defocus equivalent refraction. The latter parameter more accurately represents the refractive state of the eye because it distinguishes between eyes that have similar spherical equivalent refraction but different degrees of astigmatism.[10]

The predictability of the refractive outcome in group 1 was shown to be high up to -9.00 D of intended correction. Predictability was slightly lower in group 2, with a tendency towards undercorrection indicating a requirement for adjustment of the normogram for eyes with high myopia. According to the appropriate regression equation (Figure 3), it would be necessary to add approximately 15% to the intended refraction to achieve better results. As both groups received the same conventional ablation profile but only group 1 had additional wavefront-guided ablation,

this additional wavefront correction and the exposure time difference appear to have compensated for the 15% refractive correction required for group 2. The efficacy of both procedures was good. However, the outcome appeared to be superior for group 1, with a greater percentage of eyes achieving UCVA of 20/40 or better. Moreover, in group 1, a greater percentage of eyes gained 1 Snellen line and a lower percentage lost 1 Snellen line compared with group 2.

This study, despite the short follow-up period and the small number of eyes investigated, shows that wavefront-guided LASIK is superior to non-wavefront-guided LASIK for patients with mild to moderate myopia. The amount of higher order aberration was not measured in these patients. However, previous studies have demonstrated that conventional LASIK can increase higher order aberration and may affect the visual outcome.[11-13] Therefore, correcting wavefront aberration may counter any such increase in higher order aberration and provide a better result.

Further investigation of patients who have undergone wavefront-guided and non-wavefront–guided LASIK is required to compare the quality of vision in terms of glare and contrast sensitivity.

References

1. Mrochen M, Kaemmerer M, Seiler T. Clinical results of wavefront-guided laser in situ keratomileusis 3 months after surgery. J Cataract Refract Surg. 2001;27:201-7.
2. Nagy ZZ, Palagyi-Deak I, Kovacs A, et al. First results with wavefront-guided photorefractive keratectomy for hyperopia. J Refract Surg. 2002;18(Suppl):S620-3.
3. Panagopoulou SI, Pallikaris IG. Wavefront customized ablations with the WASCA Asclepion workstation. J Refract Surg. 2001;17 (Suppl):S608-12.
4. Mrochen M, Krueger RR, Bueeler M, et al. Aberration-sensing and wavefront-guided laser in situ keratomileusis: management of decentered ablation. J Refract Surg. 2002;18:418-29.
5. Moller-Pedersen T, Ehlers N, Hjortdal JO. [Supervision.] Ugeskr Laeger. 2002;164:619-23.
6. Thibos LN. Principles of Hartmann-Shack aberrometey. J Refract Surg. 2000;16(Suppl):S563-5.
7. Mrochen M, Kaemmerer M, Mierdel P, et al. Principles of Tscherning aberrometry. J Refract Surg. 2000;16(Suppl):S570-1.
8. Molebny VV, Panagopoulou SI, Molebny SV, et al. Principles of ray tracing aberrometry. J Refract Surg. 2000;16(Suppl):S572-5.
9. Macrae SM, Fujieda M. Slit skiascopic-guided ablation using the Nidek laser. J Refract Surg. 2000;16(Suppl):S576-80.
10. Waring GO 3rd. Standard graphs for reporting refractive surgery. J Refract Surg. 2000;16:459-66.
11. Marcos S. Aberrations and visual performance following standard laser vision correction. J Refract Surg. 2001;17(Suppl):S596-601.
12. Miller JM, Anwaruddin R, Straub J, et al. Higher order aberrations in normal, dilated, intraocular lens, and laser in situ keratomileusis corneas. J Refract Surg. 2002;18(Suppl):S579-83.
13. Moreno-Barriuso E, Lloves JM, Marcos S, et al. Ocular aberrations before and after myopic corneal refractive surgery: LASIK-induced changes measured with laser ray tracing. Invest Ophthalmol Vis Sci. 2001;42:1396-403.

Blepharophimosis Syndrome and its Association with Amblyopia and Refractive Errors in a South Indian Population

Jitendra Jethani,[1] Usha Kim,[2] Hadi Kharzei,[2] Perumalsamy Vijayalakshmi[3]
[1]Paediatric Ophthalmology and Strabismus Clinic, M&J Western Regional Institute of Ophthalmology, Civil Hospital, Ahmedabad, [2]Orbit and Oculoplasty Clinic, and [3]Paediatric Ophthalmology and Strabismus Clinic, Aravind Eye Hospitals, Madurai, India

Aim: To study refractive errors, strabismus, and amblyopia, in patients presenting with blepharophimosis ptosis epicanthus inversus syndrome.
Methods: Seventy three patients with blepharophimosis syndrome attending a tertiary eye care centre in Madurai, India, from January 1997 to January 2003 were enrolled in this retrospective interventional case series. All patients underwent complete ocular examination, which included measurement of the horizontal and vertical palpebral aperture with a ruler and measurement of levator function by Berke's method. Cycloplegic refraction and orthoptic examination were performed by a trained orthoptist.
Results: Amblyopia was present in 23 patients (31.5%) and 62 eyes (42.5%) had some form of refractive error. The latter included 30 eyes (20.5%) with high myopia. Surgical correction (frontalis sling) was performed in 63 patients (86.3%). Nine patients (12.3%) had strabismus, all of whom were children; 5 had esotropia, 2 had exotropia, and 2 had vertical deviation. All 9 patients had amblyopia.
Conclusions: Refractive errors, amblyopia, and strabismus were commonly associated with blepharophimosis syndrome. However, amblyopia was present less frequently than reported previously. A high proportion of patients were found to have high myopia.

Key words: Amblyopia, Blepharophimosis, Myopia, Refractive errors

Asian J Ophthalmol. 2007;9:68-71

Introduction

Blepharophimosis ptosis epicanthus inversus syndrome (BPES) is a congenital disorder characterised by shortening of the horizontal palpebral fissure, congenital ptosis, telecanthus, and epicanthus. Associated features are tarsal hypoplasia, tight eyelid skin, flat brow, prominent brow hair, and malar hypoplasia.[1] BPES is associated with a high prevalence of refractive errors, strabismus, and amblyopia.[2-4] This retrospective study was performed to investigate the prevalence of refractive errors, strabismus, and resultant amblyopia in a South Indian population with BPES.

Methods

Criteria for inclusion in the study were: diagnosis of BPES; minimum follow-up for 1 year at 6 monthly intervals; and records of complete examination of refractive error and amblyopia. Patients were excluded if the data were inconclusive and likely to lead to subjective bias.

The lid height (palpebral fissure distance) was observed and measured with each eye fixating on a distant target. The distance measured was the greatest width of the palpebral fissure with the patient's eyes in a straight gaze. The lid position in downgaze was noted. The extent of ptosis was determined using a ruler with the patient fixing in a straight gaze and corneal reflex in the centre. The distance measured was the margin reflex distance from the centre of the upper lid to the corneal reflex. When ptosis was unilateral, the extent of ptosis was calculated by subtracting the distance measured from the corresponding margin reflex distance of the fellow eye. When ptosis was bilateral, the value was subtracted from 5 mm (taken as normal). The extent of ptosis was used to assign a grade according to the following definitions: mild ptosis, <2 mm; moderate ptosis, 2 to 4 mm; severe ptosis, >4 mm.

After the palpebral fissure distance was measured, Berke levator function was evaluated. With the patient looking downward,

Correspondence: Dr Jitendra Jethani, M & J Western Regional Institute of Ophthalmology, Civil Hospital, Ahmedabad 380 016, India.
Tel: (91 98) 2556 0870; Fax: (91 79) 2646 1194;
E-mail: xethani@rediffmail.com

a ruler was positioned with a mark adjacent to the upper lid margin. Then, with the examiner's hand eliminating any brow action by the patient, the patient was asked to look upward as far as possible without a change in head position and the lid elevation was measured with the ruler and recorded.[5]

Certified ophthalmic technicians performed cycloplegic retinoscopy. To achieve cycloplegia, proparacaine 0.5% was instilled into the inferior cul de sac of the eye, followed 30 seconds later by a single drop of cyclopentolate 1% (or cyclopentolate 0.5% for children younger than 1 year). The eyelid was held open and the pooled drop was in contact with the cornea for approximately 1 second before the upper eyelid was lifted, allowing the pooled drop to collect under the upper eyelid. Another drop of cyclopentolate was inserted 15 to 20 minutes later using the same procedure. After waiting 20 to 30 minutes, dynamic retinoscopy was performed to determine the adequacy of cycloplegia. Dynamic retinoscopy was performed by observing the retinoscopy reflex while the patient viewed a distant target and then directing the patient to look at a finger puppet held alongside the retinoscope. Evidence of inadequate cycloplegia was shown by a shift in the retinoscopic reflex as the viewing distance changed. If cycloplegia was inadequate, another drop of cyclopentolate was instilled and the patient was re-examined 20 minutes later.

All the patients received a complete ophthalmic evaluation and orthoptic assessment at 5 days, 1 month, 6 months, and 1 year after surgery. Patients who did not undergo surgery were followed up every 6 months. All children of preschool age had cycloplegic refraction with spectacle correction, if necessary. Visual acuity was assessed according to age using preferential looking charts (Teller acuity cards) for children younger than 2 years, Keeler crowding charts for verbal children, and Snellen charts for children older than 5 years and adults. Amblyopia was defined as visual acuity less than 6/12 and/or a 2 line difference between the 2 eyes after refractive error correction and exclusion of organic pathology as a cause of reduced vision.

Frontalis sling surgery, which is designed to augment the patient's lid elevation through brow elevation,[6] was performed by one surgeon using the standard trapezoid-pentagon technique. Non-absorbable sutures (2-0 green braided polyester) were used to secure the lids to the frontalis muscles.

Results

Of the 73 patients, 38 (52%) were men and 35 (48%) were women. Patients were grouped according to their age at presentation as follows: younger than 6 years (within the amblyogenic age group), 6 to 18 years, and older than 18 years (Table 1). Approximately 50% of patients were younger than 6 years.

Table 1. Distribution of blepharophimosis syndrome according to age at presentation.

Age (years)	Number of patients (%)
<6	37 (50.7)
6 to 18	27 (37.0)
>18	9 (12.3)
Total	73

Table 2. Distribution of various refractive errors in eyes examined.

Refractive error	Number of eyes (%)
Myopia	36 (24.7)
Simple myopia (≤ -6.0 D)	6 (4.1)
High myopia (> -6.0 D)	30 (20.5)
Hypermetropia	8 (5.5)
Simple hypermetropic astigmatism	6 (4.1)
Simple myopic astigmatism	4 (2.7)
Compound hypermetropic astigmatism	4 (2.7)
Compound myopic astigmatism	0 (0)
Mixed astigmatism	4 (2.7)
Total, with refractive error	62 (42.5)
Total, no refractive error	84 (57.5)

Severe ptosis was present in 103 of the 146 eyes (70.5%): 48 patients had symmetrical bilateral severe ptosis and 7 eyes had unilateral ptosis. Moderate ptosis was present in 28 eyes (19.2%): 12 patients had bilateral symmetrical moderate ptosis and 4 had unilateral moderate ptosis. Of the 48 patients with bilateral severe ptosis, 6 had strabismus, 2 had bilateral amblyopia, and 5 had unilateral amblyopia.

Sixty two of the 146 eyes (42.5%) examined had some form of refractive error (Table 2). Thirty six eyes had myopia, mainly high myopia, and 8 had simple hypermetropia. None of the eyes had a spherical equivalent of > +3.0 D. Eighteen of the 62 eyes (29%) with refractive errors had astigmatism of various types (Table 2).

Surgery for ptosis was required for 63 patients (86.3%), 57 patients required Y-V plasty for correction of cosmetically disfiguring telecanthus, and 6 patients declined to have surgery. As indicated in Table 3, correction of ptosis was satisfactory for 49% of patients and further surgery was required by 30%, the main reasons being undercorrection, asymmetrical correction, or complications such as suture granuloma.

The visual acuity of all patients is summarised in Table 4. Twenty three patients (31.5%) had amblyopia. Four patients had bilateral amblyopia and 19 had unilateral amblyopia. Amblyopia was severe

Table 3. Outcome for 63 patients who underwent surgery for ptosis.

Surgical outcome	Number of patients (%)
Good	31 (49.2)
Fair (no further surgery)	13 (20.6)
Further surgery needed	
For complications	5 (26.3)
Asymmetrical or undercorrection	14 (73.6)

Table 4. Visual acuity of all patients.

Visual acuity	Number of patients (%)
Symmetrical, both eyes	
6/6 to 6/9	46 (63.0)
6/12 to 6/18	2 (2.7)
6/24 to 6/60	2 (2.7)
Total	50 (68.4)
Asymmetrical, worse eye	
Cataract	4 (5.5)
6/12 to 6/18	2 (2.7)
6/24 to 6/60	10 (13.7)
<6/60	7 (9.6)
Total	23 (31.5)

(visual acuity <6/60 in the worse eye) in 7 patients. The 4 patients with visually significant cataracts were excluded from the amblyopia analysis.

Of the 23 children with amblyopia, 9 had strabismus associated with ptosis, 6 had anisometropia, and the remainder had no significant refractive error. Of the 4 patients with bilateral amblyopia, 2 had severe ptosis and 2 had refractive errors with moderate and mild ptosis. Nine children (12.3%) had strabismus: 5 had esotropia, 2 had exotropia, and 2 had vertical deviation. Amblyopia was also present in 9 children with strabismus, 4 of whom (6 eyes) had some form of refractive error; 3 of the 4 children had unilateral amblyopia and 1 had bilateral amblyopia. Twelve patients (16.4%) had autosomal dominant inheritance.

Discussion

Von Ammon first reported blepharophimosis in 1841.[7] Defects observed with blepharophimosis include asymmetry of the ears, flat nasal bridge, flat face, mongolism, dwarfism, and oligophrenia.[1] Eye defects associated with congenital blepharophimosis include strabismus, nystagmus, amblyopia, microphthalmos, anophthalmos, ptosis, epicanthus, inverse epicanthus, microcornea, and hypermetropia.[8] Calmettes et al reported that patients with macular heterotropia had associated blepharophimosis.[9] Dawson et al, in a study of 204 patients with BPES, found that 34% had significant refractive error requiring spectacles.[4] Of these, 30% had anisometropic hypermetropia and 34% had anisometropic myopia. Overall, hypermetropia was present in 43% of patients and 7% had myopia. Significant astigmatism was found in 40% of patients, but this did not increase the risk of amblyopia.[4] Based on their findings, Dawson et al stressed that patients with severe ptosis should undergo correction before the age of 3 years and that all other patients should undergo surgery before the age of 5 years.[4]

In the present study, 42% of eyes had some form of refractive error, which is comparable to the results of other studies. However, analysis of the types of refractive errors present showed that a large number of patients (20.5%) had high myopia (>6.0 D). A study by Raju et al suggested that 3.7% of the South Indian population had high myopia, with a prevalence of 4.3% after age and gender adjustment.[10] A significantly higher proportion of patients had high myopia in the present study. However, it is not clear whether this condition is secondary to BPES or a coexisting feature.[10]

The risk of amblyopia associated with BPES has been the focus of much research. Beaconsfield et al reported a high risk of amblyopia (56.4% of the 101 patients investigated).[2] In a study by Dawson et al, 40.6% of the patients had amblyopia, either bilaterally or unilaterally,[4] while Beckingsale et al found an amblyopia rate of 39% among 28 patients investigated.[3] In the present series, only 31.5% of the patients had amblyopia. All of these studies clearly implicate BPES as a cause of amblyopia, although the present study shows the lowest incidence of amblyopia. It seems appropriate to include refractive error as part of this syndrome. Amblyopia may be due to refractive error or due to form visual deprivation secondary to ptosis and blepharophimosis.

Dawson et al reported that 20% of patients with BPES had manifest strabismus,[4] compared with 12.3% in this study. A striking feature of the present study is the finding that 90% of patients with strabismus had amblyopia. It is clear that the presence of refractive error together with strabismus increases the risk for amblyopia.

In BPES, the surgical correction of significant ptosis is required as early as possible. However, this study indicates that refractive errors are an equal or greater cause of amblyopia, with a high prevalence of high myopia. Therefore, early prescription of glasses will assist greatly in preventing amblyopia. Refractive errors should be regarded as a significant aspect of this syndrome. The presence of strabismus appears to increase the risk for amblyopia, which increases even more in the presence of refractive errors. However, the amount of ptosis alone may not be sufficient to cause amblyopia in all patients.

References

1. Conlon Ronan M, Sutula FC. Congenital lid anomalies. In: Albert D, Jacobiec FA, editors. Principles and practice of ophthalmology. 2nd ed. Philadelphia: WB Saunders; 2000. p. 3331-3.
2. Beaconsfield M, Walker JW, Collins JR. Visual development in blepharophimosis syndrome. Br J Ophthalmol. 1991;75:746-8.
3. Beckingsale PS, Sullivan TJ, Wong VA, et al. Blepharophimosis: a recommendation for early surgery in patients with severe ptosis. Clin Experiment Ophthalmol. 2003;31:138-42.
4. Dawson EL, Hardy TG, Collin JR, et al. The incidence of strabismus and refractive error in patients with blepharophimosis, ptosis and epicanthus inversus syndrome (BPES). Strabismus. 2003;11:173-7.
5. Meyer DR, Rheeman CH. Downgaze eyelid position in patients with blepharoptosis. Ophthalmology. 1995;102:1517-23.
6. Fox SA. Complications of frontalis sling surgery. Am J Ophthalmology. 1967;63:758-62.
7. Von Ammon FA. Klinische Darstellung der Krankheiten des Auges

and Augenlider. Berlin: G Reimer; 1841.
8. Schwartz O, Jampel RS. Congenital blepharophimosis syndrome associated with a unique generalized myopathy. Arch Ophthalmol. 1962;68:52-7.
9. Calmettes L, Deodati F, Amalric P. [Macular heterotropia with blepharophimosis in two generations.] Bull Soc Belge Ophtalmol. 1957;114:516-25.
10. Raju P, Ramesh SV, Arvind H, et al. Prevalence of refractive errors in a rural South Indian population. Invest Ophthalmol Vis Sci. 2004; 45:4268-72.

Colour Doppler Imaging Analysis of Ocular Blood Flow Velocity and Resistive Index in Glaucoma Patients

Dilip Pandit, Sunita Unercat, Ramesh Agrawal
Mumbai Port Trust Hospital, Mumbai, India

Aim: *To use colour Doppler imaging to study the blood flow velocity and resistive index in the central retinal and short posterior ciliary arteries of patients with glaucoma.*
Methods: *Blood flow velocity and resistive index were assessed by colour Doppler imaging in 40 patients with primary open angle glaucoma, 40 patients with normal tension glaucoma, and a control group of 20 individuals without glaucoma. The mean peak systolic velocity, end diastolic velocity, and resistive index were measured in each patient.*
Results: *In the central artery, the mean peak systolic velocity and end diastolic velocity were significantly lower in the patients with primary open angle glaucoma and normal tension glaucoma than in the control group. No significant changes in any parameter were detected in the short posterior medial and lateral ciliary arteries in the patients with primary open angle glaucoma compared with controls, but there were significant decreases in end-diastolic velocity in the patients with normal tension glaucoma. Generally, the resistive index tended to be higher in patients with glaucoma than in controls, most noticeably in the central retinal artery, but the differences were not statistically significant. There were no significant differences between the 2 groups of patients with glaucoma.*
Conclusion: *Open angle glaucoma was associated with a decrease in both peak systolic and end diastolic velocity and a possible increase in the resistive index in the ocular vasculature, predominantly in the central retinal artery. Colour Doppler imaging appears to be a useful modality for studying ocular haemodynamics.*

Key words: *Blood flow velocity, Ciliary arteries, Color Doppler ultrasonography, Glaucoma*

Asian J Ophthalmol. 2007;9:72-5

Introduction

Glaucoma is a syndrome of progressive optic neuropathy characterised by optic nerve excavation and visual field defects. Although elevated intraocular pressure (IOP) is the main cause of such damage, the existence of normal tension glaucoma (NTG) and the weak correlation between progression and IOP values[1,2] indicate that other factors may also be involved in the pathogenesis of glaucomatous damage, which can occur at virtually any IOP level.

The main predisposing factors reported in the literature include not only age and genetic and demographic factors but also vascular and rheologic factors.[3,4] Colour Doppler imaging allows information about the flow of blood to be superimposed in colour on a B-mode grey scale ultrasound image, enabling direct visualisation of specific vessels. The blood velocity is calculated from the spectral display. Peak systolic velocity (PSV) and end diastolic velocity (EDV) measured in this way are used to calculate the resistive index according to the method of Pourcelet, where resistive index = PSV-EDV/PSV.[5] Resistive index represents a measure of end organ resistance.

In this study, the reproducibility of colour Doppler imaging for the measurement of blood flow velocity in the central retinal artery and medial and lateral short posterior ciliary arteries was assessed in 3 study populations: patients with primary open angle glaucoma (POAG), patients with NTG, and a control group.

Correspondence: Dr Sunita Unercat, 3, Charak, Mumbai Port Trust Hospital Compound, Wadala (East), Mumbai 37, India.
Tel: (91 22) 6656 7923; Fax: (91 22) 2414 5115;
E-mail: cmo@mbptmail.com

Methods

Patients

Patients with newly diagnosed POAG or NTG, aged 40 to 70 years, were recruited into the study. The inclusion criteria were as follows. A diagnosis of POAG based on IOP >21 mm Hg with indentation tonometry on 3 consecutive visits, open angle by gonioscopy, and optic nerve head and visual field changes characteristic of glaucoma (40 patients). A diagnosis of NTG based on IOP <21mm Hg

on 3 consecutive visits, open angle on gonioscopy, and typical optic nerve head and visual field changes (40 patients). The control group consisted of 20 individuals, age- and sex-matched to the glaucoma groups, with IOP <21 mm Hg, normal angle, no visual field and optic nerve head changes, and no family history of glaucoma.

Exclusion criteria for all groups were any prior ocular surgery or ocular disorder (including secondary glaucoma) or any condition preventing reliable tonometry and visual field assessment. None of the patients were receiving any topical or systemic medication affecting vascular tone and flow or IOP. All participants consented to and underwent colour Doppler imaging for blood flow velocity in the central retinal artery and the medial and lateral short posterior ciliary arteries.

Colour Doppler Imaging

All colour Doppler ultrasound studies were performed by a single experienced sonologist using a Philips HDI 5000 system (Seattle, USA).Broadband linear array high-frequency 5 to 12 mHz was used for grey scale imaging of the globe. All examinations were carried out in the supine position with the eyes closed. Each eye was examined in B-scan mode in both the transverse and sagittal plane. Colour Doppler settings were adjusted to detect slow flow in the central retinal and posterior ciliary vessels. Using the colour flow as a map, the central retinal artery was identified and interrogated in the centre of the optic nerve head shadow as close to the retinal surface as possible. At least 2 separate spectral samples of each vessel were collected. The short posterior ciliary arteries were interrogated in the nasal and temporal position adjacent to the optic nerve immediately posterior to the sclera with the probe in the transverse plane. Features of the scan included appropriate sampling site, appropriate angle correction, clarity of the spectral image and noise content, and accurate velocity measurements. Typical colour Doppler scans are shown in Figures 1 and 2.

Figure 1. Spectral wave form of central retinal artery showing peak systolic velocity 11.3 cm/second, end diastolic velocity 3.6 cm/second, and resistive index 0.68.

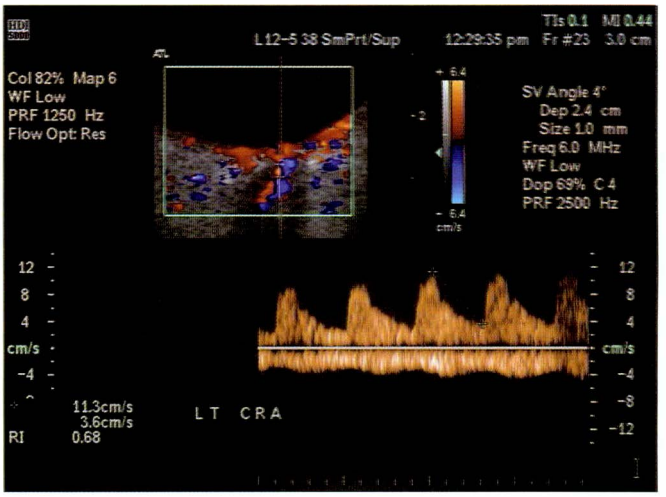
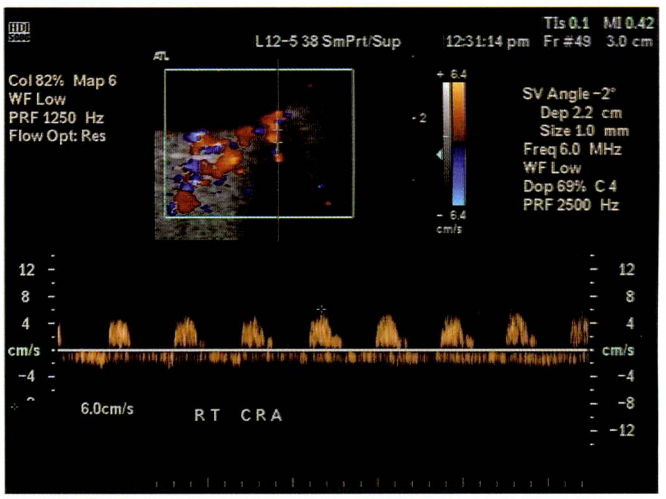


Figure 2. Spectral wave form of central retinal artery showing peak systolic velocity 6.0 cm/second, end diastolic velocity 0 cm/second, and resistive index 1.0.



Results

There was no significant difference between the 3 study groups with respect to age and sex. The mean PSV, EDV, and resistive index in the central retinal artery and medial and lateral short posterior ciliary arteries are given for the right and left eyes of all participants in Tables 1, 2, and 3, respectively, together with p values obtained by applying Student's unpaired *t* test. A p value of <0.05 was considered significant.

In the central artery (Table 1), the mean PSV and EDV were significantly lower for the patients with POAG and NTG than for the control group, with no significant difference between patients in the 2 glaucoma groups. There was an apparent increase in the mean resistive index in both glaucoma groups compared with the control group but this was not statistically significant.

In the medial posterior ciliary artery (Table 2) and lateral posterior ciliary artery (Table 3), the mean PSV and mean resistive index for the patients with POAG and NTG were not significantly different from corresponding values for the control group. However, in both these arteries and in the right eye only, the mean EDV was found to be significantly lower for patients in the NTG group than for the control group (Tables 2 and 3).

Discussion

Colour Doppler imaging and spectral analysis are attractive tools for non-invasive vascular investigation of retrobulbar vessels. The central retinal artery is easily identified and measurements of this vessel are the most reproducible because of its position in the optic nerve head and characteristic wave form (Figure 1). Measurements

Table 1. Mean blood flow velocity in the central retinal artery.

	Mean (SD)			p Value		
	Control (n = 20)	POAG (n = 40)	NTG (n = 40)	Control vs POAG	Control vs NTG	POAG vs NTG
Right eye						
PSV [cm/second]	9.6 (1.24)	8.29 (1.88)	8.12 (2.43)	0.003	0.003	0.73
EDV [cm/second]	2.56 (1.04)	1.30 (1.48)	1.44 (1.61)	0.002	0.002	0.69
RI	0.80 (0.14)	0.82 (0.16)	0.85 (0.15)	0.64	0.22	0.39
Left eye						
PSV [cm/second]	9.85 (1.86)	8.18 (2.28)	7.86 (2.02)	0.006	0.001	0.52
EDV [cm/second]	2.46 (1.36)	1.27 (1.28)	1.23 (1.30)	0.002	0.002	0.86
RI	0.81 (0.16)	0.84 (0.14)	0.86 (0.15)	0.47	0.24	0.55

Abbreviations: POAG = primary open angle glaucoma; NTG = normal tension glaucoma; PSV = peak systolic velocity; EDV = end diastolic velocity; RI = resistive index.

Table 2. Mean blood flow velocity in the medial short posterior ciliary artery.

	Mean (SD)			p Value		
	Control (n = 20)	POAG (n = 40)	NTG (n = 40)	Control vs POAG	Control vs NTG	POAG vs NTG
Right eye						
PSV [cm/second]	8.09 (2.41)	8.02 (1.14)	7.69 (1.73)	0.87	0.84	0.89
EDV [cm/second]	2.79 (0.52)	2.59 (1.19)	2.33 (0.68)	0.37	0.01	0.23
RI	0.64 (0.09)	0.67 (0.12)	0.67 (0.09)	0.33	0.23	0.95
Left eye						
PSV [cm/second]	7.38 (1.79)	7.57 (2.75)	7.82 (2.51)	0.69	0.45	0.68
EDV [cm/second]	2.44 (0.74)	2.29 (0.57)	2.37 (1.02)	0.39	0.78	0.67
RI	0.67 (0.08)	0.68 (0.09)	0.69 (0.07)	0.45	0.22	0.49

Abbreviations: POAG = primary open angle glaucoma; NTG = normal tension glaucoma; PSV = peak systolic velocity; EDV = end diastolic velocity; RI = resistive index.

Table 3. Mean blood flow velocity in the lateral short posterior ciliary artery.

	Mean (SD)			p Value		
	Control (n = 20)	POAG (n = 40)	NTG (n = 40)	Control vs POAG	Control vs NTG	POAG vs NTG
Right eye						
PSV [cm/second]	7.66 (0.87)	7.81 (2.6)	7.90 (2.26)	0.74	0.56	0.84
EDV [cm/second]	2.59 (0.60)	2.34 (1.06)	2.14 (0.52)	0.25	0.004	0.29
RI	0.69 (0.07)	0.69 (0.10)	0.71 (0.08)	0.95	0.35	0.33
Left eye						
PSV [cm/second]	7.67 (1.01)	7.78 (2.43)	7.44 (2.02)	0.79	0.57	0.51
EDV [cm/second]	2.01 (1.20)	1.91 (0.66)	2.17 (0.92)	0.71	0.60	0.15
RI	0.74 (0.15)	0.73 (0.09)	0.70 (0.10)	0.78	0.29	0.16

Abbreviations: POAG = primary open angle glaucoma; NTG = normal tension glaucoma; PSV = peak systolic velocity; EDV = end diastolic velocity; RI = resistive index.

of velocity in the central retinal artery are considered more accurate than those in the short posterior ciliary arteries because it is difficult to follow the course of the latter vessels and accurately angle the ultrasound beam within them. Despite this limitation, blood velocity is probably a reasonable indicator of blood flow within these vessels.[6,7]

Colour Doppler measurements of velocity in the short posterior ciliary arteries have been reported previously.[8-10] Galassi et al[9] noted an increase in the resistive index in patients with glaucoma and Trible et al[10] noted an increase in diastolic velocity and a decrease in resistive index in patients with glaucoma following trabeculectomy. In the present study, although there were significant differences in central retinal artery indices of patients with glaucoma compared with the corresponding values for controls, the short posterior ciliary arteries only showed a significant difference in patients with NTG.

Although there is a significant difference in blood flow velocities between patients with glaucoma and controls, it is not clear whether the vascular changes are primary or secondary to optic nerve damage. The difference merely indicates a compromised vascular supply in the region in patients with glaucoma. The vascular changes, if primary, may play a role in the pathogenesis of glaucomatous damage; if secondary, they may be associated with structural changes in the optic nerve head. To establish the role of these vascular changes in the pathogenesis of glaucoma, longitudinal studies of glaucoma suspects and patients with early disease are needed.

Quantitative measurements of velocity and resistive index are useful for comparing study populations. In the assessment of an individual, critical analysis of spectral waveform is often informative. In the spectral waveform for the central retinal artery shown

in Figure 2, the systolic peak is rounded and the EDV is not measurable. The systolic peak rounding is indicative of proximal disease leading to loss of sharp systolic upstroke. Loss of EDV leads to a marked increase in the resistive index and a low EDV may be critical when perfusion is already compromised.

In conclusion, this study demonstrates a significant decrease in mean EDV and PSV in the central retinal artery in patients with newly diagnosed POAG and NTG. The only significant change observed in the short posterior ciliary arteries in these patients was a reduction in the mean EDV in the patients with NTG compared with controls.

These findings illustrate the use of colour Doppler imaging to assess changes that occur in the optic nerve head vascular supply in patients with glaucoma. In the future, it may be useful to investigate colour Doppler parameters in relation to the degree of damage and its site in patients with varying degrees of glaucomatous damage.

References

1. Chumbley LC, Brubaker RF. Low tension glaucoma. Am J Ophthalmol. 1976;81:761-7.
2. Drance SM, Sweeney VP, Morgan RW, et al. Study of factors involved in the production of low tension glaucoma. Arch Ophthalmol. 1973;89: 457-65.
3. Kaiser HJ, Flammer J, Graf T, et al. Systemic blood pressure in glaucoma patients. Graefes Arch Clin Exp Ophthalmol. 1993;231: 671-80.
4. Hayreh SS, Zimmerman MB, Podhajsky P, et al. Nocturnal arterial hypotension and its role in optic nerve head and ocular ischemic disorders. Am J Ophthalmol. 1994;117:603-24.
5. Planiol T, Pourcelot L, Pottier JM, et al. Etude de la circulation carotidienne par les methods ultrasoniques et la thermographic. Rev Neurol (Paris). 1972;126:127-41.
6. Taylor GA, Short BL, Walker LK, et al. Intracranial blood flow: quantification with duplex Doppler and color Doppler flow US. Radiology. 1990; 176:231-6.
7. Hansen NB, Stonestreet BS, Rosenkrantz TS, et al. Validity of Doppler measurements of anterior cerebral artery blood flow velocity: correlation with brain blood flow in piglets. Paediatrics. 1983;72:526-31.
8. Augustyniak KE, Swietliczko I, Aaslid R. [Evaluation of blood flow velocity and pulsation curve in the posterior ciliary arteries in glaucoma.] Klin Oczna. 1989;91:3-6.
9. Galassi F, Nuzzaci G, Sodi A, et al. Color Doppler imaging in evaluation of optic nerve blood supply in normal and glaucomatous subjects. Int Ophthalmol. 1992;16:273-6.
10. Trible JR, Sergott RC, Spaeth GL, et al. Trabeculectomy associated with retrobulbar hemodynamic changes. A — color Doppler analysis. Ophthalmology. 1994;101:340-51.

Manifestations of Progressive Herpes Simplex Virus Endotheliitis

Somasheila I Murthy,[1,2] Virender S Sangwan,[1,2] Sushma Tejwani,[3] Sreedharan Atmanathan,[4] Gullapalli N Rao[1]

[1]Cornea and Anterior Segment Services, [2]Department of Ocular Immunology and Uveitis, [3]Comprehensive Ophthalmology Services, and [4]Jhaveri Microbiology Centre and Professor Brien Holden Eye Research Centre, LV Prasad Eye Institute, Hyderabad, India

Aim: *To study the manifestations of progressive herpes simplex virus endotheliitis.*

Methods: *The records of 10 eyes of 6 patients diagnosed with herpes simplex virus endotheliitis were reviewed in this retrospective case series. All patients attended the LV Prasad Eye Institute between August 1997 and May 2001. Data collection included patients' demographics, clinical details, and virological investigations. The clinical course, laboratory investigations, management, and outcome are described.*

Results: *There were 4 men and 2 women (median age, 23.5 years; range, 10 to 66 years). Four patients had bilateral involvement, 2 of whom had simultaneous onset. Best corrected visual acuity at presentation ranged from perception of hand movements to 20/50. Progressive features included bilateral severe visual loss (7 eyes), epithelial defect (5 eyes), anterior stromal infiltrate (5 eyes), and severe uveitis with hypopyon (5 eyes). Polymerase chain reaction for HSV-1 DNA was positive in 4 of 6 patients. All patients were treated with corticosteroids and acyclovir. Final visual acuity of 20/30 or better was achieved in 6 of the 10 eyes. Complications encountered were dense corneal scarring with vascularisation (4 eyes), secondary bacterial keratitis (2 eyes), and total corneal melt (1 eye). Three eyes underwent penetrating keratoplasty, with graft failure in 2 eyes.*

Conclusions: *Clinical manifestations of herpes simplex virus endotheliitis vary from mild to severe disease. Progressive presentation includes unilateral or bilateral corneal oedema and severe uveitis with epithelial defects and stromal infiltrates mimicking bacterial keratitis. Polymerase chain reaction for herpes simplex virus may be a valuable tool for confirming viral aetiology.*

Key words: *Herpes simplex virus, Herpetic keratitis, Polymerase chain reaction, Signs and symptoms, Viral eye infections*

Asian J Ophthalmol. 2007;9:76-81

Introduction

Herpes simplex virus (HSV) keratitis is a leading cause of corneal blindness.[1] HSV is a complex disease, caused by both live viral infection and immune and inflammatory response–related damage to the ocular structures.[2] The clinical presentation is protean and all layers of the cornea may be involved. While both epithelial and stromal keratitis are easily diagnosed, it is only recently that HSV endotheliitis has gained recognition as a distinct clinical entity.[3] This study represents a case series of patients with varied clinical manifestations and a subsequent diagnosis of HSV endotheliitis based on both clinical presentation and laboratory investigations.

Correspondence: Dr Somasheila I Murthy, LV Prasad Eye Institute, LV Prasad Marg, Banjara Hills, Hyderabad, Andhra Pradesh, 500 036, India. Tel: (91 40) 3061 2630; Fax: (91 40) 2354 8271; E-mail: smurthy@lvpei.org

Methods

The records of 6 patients whose final diagnosis was HSV endotheliitis were reviewed. All patients attended the LV Prasad Eye Institute in Hyderabad, India, between August 1997 and May 2001. Data collection included patients' demographics, clinical details, and virological investigations. Various ocular specimens (aqueous fluid, corneal scrapings, and corneal button) underwent polymerase chain reaction (PCR) analysis for detection of HSV-1 DNA using primers that specifically amplify a 221 base pair sequence of the gene coding for HSV-1 glycoprotein D and a modification of a method described previously.[4]

Results

The median age of the patients was 23.5 years (range, 10 to 66 years). There were 4 men and 2 women. Bilateral disease was

Table 1. Slit-lamp examination at presentation.

Patient number/eye	Epithelium	Stromal oedema	Stromal infiltrates	Descemet folds	Endothelial exudates	Keratic precipitates	Anterior chamber reaction	Hypopyon (mm)	Other
1 Right	Defect	Diffuse	-	+	++	++	2+	1	-
1 Left	Defect	Disciform	+	+	++	++	2+	1	Cataract
2 Right	Oedema	Diffuse	-	+	-	++	2+	-	-
3 Right	-	Diffuse	-	+	-	+	2+	-	Raised intraocular pressure
4 Right*	-	Disciform	-	+	-	++	Poor view	-	-
4 Left*	-	Diffuse	-	+	-	++	Poor view	-	-
5 Right	Defect	Diffuse	+	+	-	++	Poor view	2	-
5 Left	Defect	Diffuse	+	+	++	++	2+	2	-
6 Right*	-	Sectoral	+	+	-	+	2+	-	-
6 Left*	Defect	Sectoral	+	+	+ (ring)	+	2+	<1	-
Number affected	5/10	6/10†	5/10	All	4/10	All	All	5/10	

* Simultaneous onset.
† Diffuse oedema.

present in 4 patients, 2 of whom had simultaneous onset of symptoms in both eyes. Presenting best-corrected visual acuity (BCVA) ranged from hand movements to 20/50 and 4 patients complained of severe visual loss at initial presentation, with visual acuity of counting fingers or less.

The results of the slit-lamp examination at presentation are summarised in Table 1. Stromal oedema, which was present in all patients, was diffuse in 6 of the 10 eyes, disciform in 2 eyes, and sectoral in 2 eyes. Epithelial defects and stromal infiltrates were detected in 5 eyes and Descemet's folds were present in all eyes. The endothelium showed exudates in 4 eyes and keratic precipitates in all eyes. Anterior chamber reaction could be evaluated in 7 eyes and was severe in each case, with hypopyon present in 5 eyes.

The treatment, outcome, and complications for each patient are summarised in Table 2, together with the results of virological investigations. HSV-1 DNA was detected by PCR in 4 of the 6 patients.

All patients were treated with a combination of oral and topical acyclovir and corticosteroids. Two patients with bilateral simultaneous involvement were also treated with intravenous methylprednisolone (Table 2; patients 4 and 6). Complications encountered were cataracts, secondary bacterial infection, and total corneal melt (Table 2). Three eyes underwent penetrating keratoplasty but 2 of the grafts failed.

The keratitis resolved with formation of avascular scars in 5 of 10 eyes, dense vascularised scars in 4 of 10 (of which 2 underwent penetrating keratoplasty), and corneal melt in 1 eye, which eventually resulted in phthisis bulbi. Six eyes regained visual acuity of 20/30 or better while 4 eyes had poor final visual acuity ranging from light perception to 20/200.

Patients 1 and 6 are described in detail to highlight the variations in clinical presentation, course, and outcome associated with HSV endotheliitis.

Patient 1

A 38-year-old man presented in August 1997 with a 10-day history of decreased vision, redness, and pain in the left eye. BCVA was 20/20 in the right eye and hand movements in the left eye. Examination of the left eye (Figure 1) showed conjunctival injection (4+). The cornea showed an epithelial defect measuring 3.5 x 7.0 mm, diffuse stromal oedema, granular anterior stromal infiltrates, Descemet's folds, and keratic precipitates. The anterior chamber showed trace hypopyon and the lens was intumescent. The intraocular pressure was 6 mm Hg. B-scan ultrasonography revealed an echo-free vitreous cavity with attached retina and no choroidal thickening.

Although microbial keratitis was suspected, microbiological tests were negative. Empirical therapy was commenced with ciprofloxacin 0.03% eye drops half hourly, atropine 1% eye drops 8 hourly, and lubricants. Although the epithelial defect healed, the stromal infiltrates, corneal oedema, and anterior chamber reaction persisted. Betamethasone 0.1% eye drops were commenced and the dose was tapered over 2 months. During the next 5 months, the oedema gradually resolved with neovascularisation and scarring (Figure 2). Subsequently, the patient underwent cataract extraction with intraocular lens implantation in the left eye but had minimal visual improvement due to a dense stromal scar.

Nine months after initial presentation, the patient presented with a sudden decrease in vision in the right eye. BCVA was counting fingers at 1 m. Slit-lamp examination of the right eye revealed punctate epithelial erosions, diffuse stromal oedema, multiple Descemet's folds, and large keratic precipitates. The anterior chamber showed 1 mm hypopyon (Figure 1). B-scan ultrasonography was normal.

The occurrence of a similar episode previously in the left eye, which did not respond to antibiotics but healed with

Table 2. Clinical profile: treatment and outcome.

Patient number/ eye	Initial visual acuity	Polymerase chain reaction assay for herpes simplex virus-1 DNA, site of specimen	Medication	Intermediate complications	Surgery	Final visual acuity	Final outcome
1 Right	CF	+, corneal button	Oral acyclovir, oral/topical steroid, cyclopentolate	Dense vascularised scar	ECCE + PCIOL, PKP	20/25	Clear graft
1 Left	HM	-, corneal button	Topical steroid, cyclopentolate, ciprofloxacin	Dense vascularised scar	ECCE + PCIOL, PKP	CF 1 m	Failed graft
2 Right	20/60	-, AC tap +, corneal scraping +, corneal button	Oral acyclovir, oral/topical steroid, cyclopentolate	Corneal melt, perforation, bacterial keratitis	Tectonic PKP	Inaccurate projection	Retinal detachment, failed graft
3 Right	CF	+, AC tap	Oral acyclovir, oral/topical steroid, cyclopentolate, timolol maleate	Nil	Nil	20/30	Small corneal scar
4 Right	HM	-, AC tap	Pulse methylprednisolone, oral acyclovir, oral/topical steroid, homatropine	Reactivation on steroid taper	Nil	20/20	Residual corneal scar
4 Left	HM	None	As for right eye	Nil	Nil	20/20	Residual corneal scar
5 Right	20/80	-, corneal scraping	Oral/topical steroid, topical acyclovir	Nil	Nil	20/200	Dense vascularised scar
5 Left	CF	-, corneal scraping	Oral and topical acyclovir, topical steroid, atropine	Secondary bacterial keratitis treated with ciprofloxacin	Nil	HM	Dense vascularised scar, awaiting PKP
6 Right	20/50	None	Pulse methylprednisolone, oral and topical acyclovir, oral and topical steroid, homatropine	Nil	Nil	20/20	Trace scar
6 Left	CF	+, corneal scraping +, AC tap	As for right eye	Nil	Nil	20/25	Linear scar

Abbreviations: CF = counting fingers at 1 m; HM = hand movements; AC = anterior chamber; ECCE = extracapsular cataract extraction; PCIOL = posterior chamber intraocular lens; PKP = penetrating keratoplasty.

neovascularisation and scarring, suggested the possibility of HSV endotheliitis in the right eye. In view of the severity of inflammation, the following treatment was commenced: topical prednisolone 1% eye drops hourly and oral prednisolone (1 mg/kg body weight) with topical acyclovir 2% eye ointment 5 times daily, and oral acyclovir 800 mg once daily. There was gradual resolution of oedema with resultant scarring and deep vascularisation. The dose of topical steroids was tapered over a 3-month period. Oral

Figure 1. Patient 1. (a) Left eye at presentation showing large epithelial defect and disciform stromal oedema and infiltrate; and (b) right eye 9 months after first visit showing diffuse corneal oedema, Descemet's folds, and keratic precipitates.

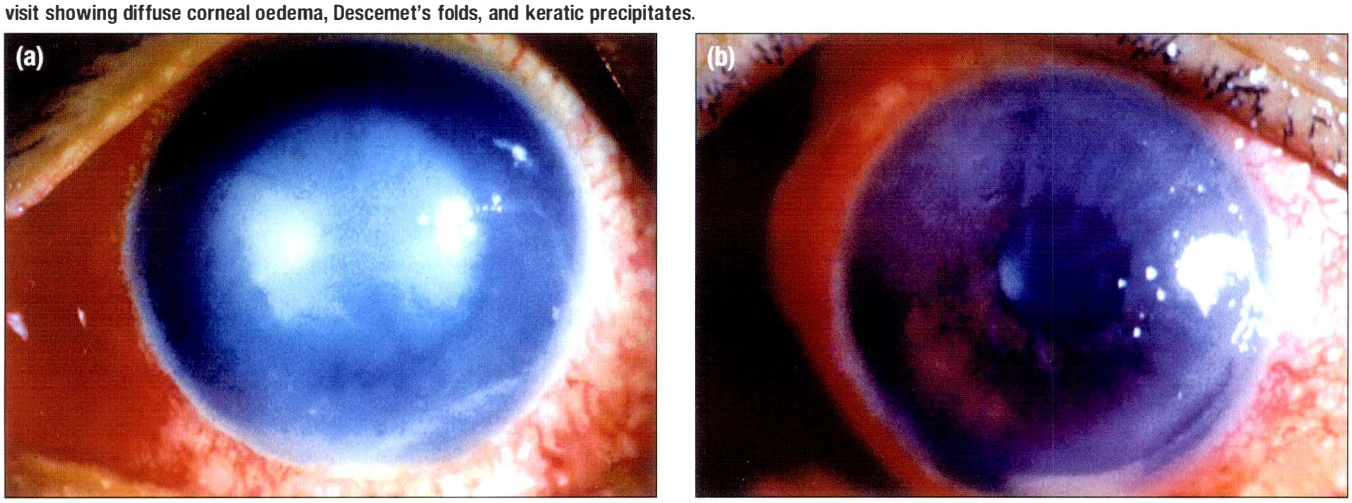
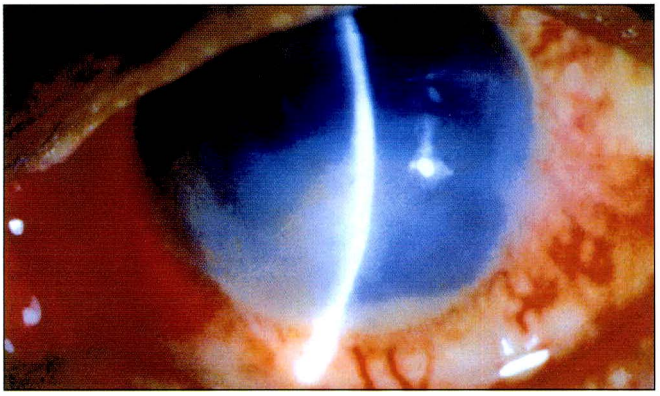


Figure 2. Patient 1. Left eye 6 weeks after treatment showing dense stromal scarring with vascularisation.



acyclovir 400 mg once daily was continued as prophylaxis against recurrence. The patient underwent uneventful cataract extraction with intraocular lens implantation in the right eye in November 1998 with only marginal improvement in vision due to corneal scarring (Figure 3a).

After a disease-free period of almost 2 years, penetrating keratoplasty was performed in the left eye. However, postoperative graft oedema persisted leading to primary graft failure. Virological investigations of the corneal button were negative. Histopathology was also unremarkable. Two and a half years after initial presentation, penetrating keratoplasty was performed in the right eye. The corneal button was assessed by PCR and immunohistochemistry and found to be positive for HSV-1 DNA and HSV-1 antigen, respectively. Oral acyclovir 800 mg once daily was continued for 1 year post-transplantation. At the patient's last visit in November 2003, BCVA was 20/25 in the right eye (Figure 3b) and 20/400 in the left eye. Repeat penetrating keratoplasty in the left eye was recommended but the patient refused and was subsequently lost to follow-up.

Patient 6

A 10-year-old boy was referred in May 2001 with a diagnosis of interstitial keratitis. He had experienced sudden onset of pain, watering, and severe photophobia in the left eye 3 weeks earlier, following an episode of a flu-like illness. He was being treated with acyclovir 2% eye ointment 5 times daily, timolol maleate 0.5% eye drops twice daily, and atropine 1% eye drops once daily.

BCVA was 20/50 in the right eye and counting fingers at 1 m in the left eye. Intraocular pressure was normal. Slit-lamp examination of the right eye showed an intact epithelium, sectoral oedema (2+), multiple cellular infiltrates in the stroma, and keratic precipitates in the affected area. Anterior chamber examination revealed cells (2+) and flare. The left cornea showed a small central (1 x 1 mm) epithelial defect, diffuse stromal oedema (1+), and a deep stromal infiltrate measuring 4.5 x 3.5 mm, an incomplete immune ring, trace hypopyon and flare (2+), and cells in the anterior chamber (Figure 4a). Based on previous experience, HSV endotheliitis was strongly suspected. Corneal scrapings and anterior chamber fluid obtained from the left eye underwent PCR and HSV-1 DNA was detected in both samples.

Considering the severity of the disease, therapy was initiated with 3 infusions of intravenous methylprednisolone 150 mg over 3 days, followed by oral prednisone 1 mg/kg tapered over the following 6 weeks. Topical treatment included acyclovir 2% eye ointment 5 times daily, prednisolone acetate 1% eye drops 2 hourly, and cyclopentolate 1% eye drops 3 times daily. Oral acyclovir 400 mg 5 times daily was also given.

After 1 week, there was significant improvement. The lesions completely resolved over a 1-month period and the medications were tapered and discontinued over the next 3 months. BCVA improved to 20/25 in both eyes with faint residual corneal scars

Figure 3. Patient 1. Right eye (a) prior to keratoplasty showing stromal scar; and (b) at last follow-up showing a clear graft.

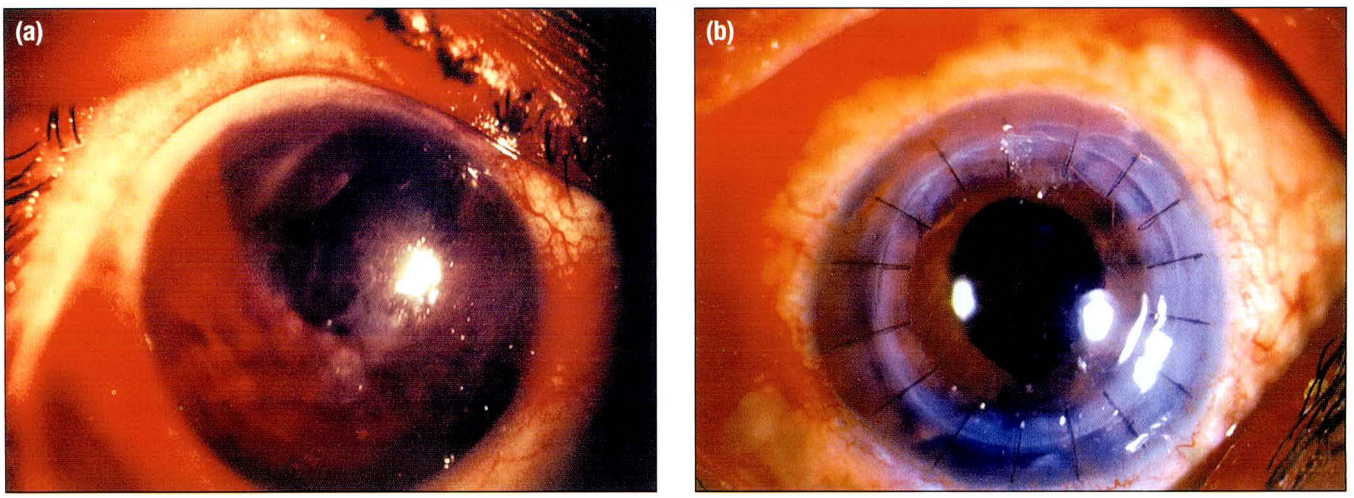
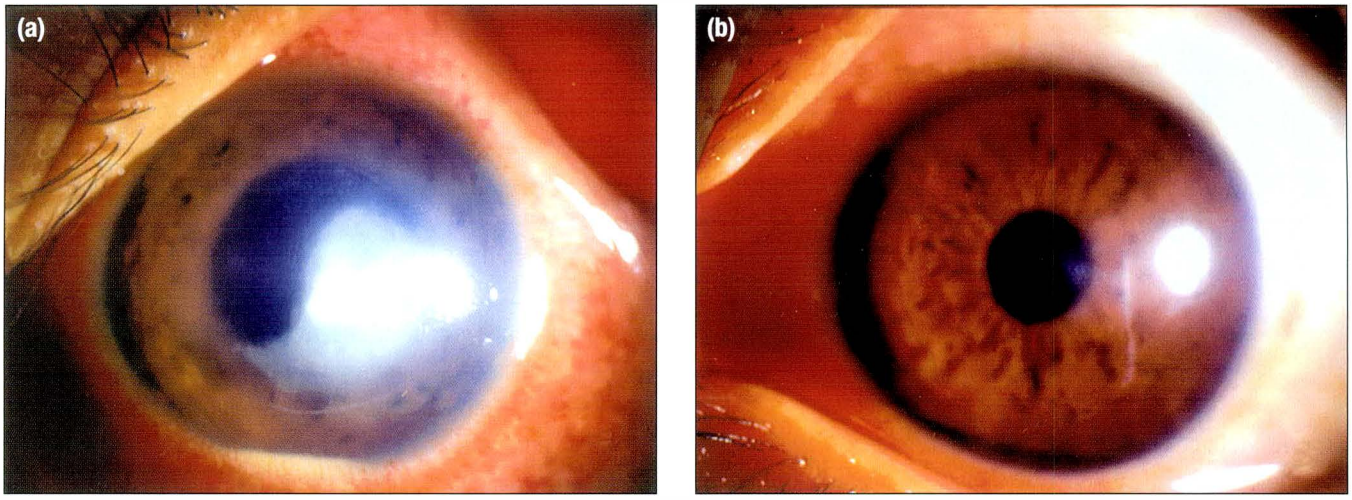


Figure 4. Patient 6. Left eye (a) at presentation showing central dense oedema, patchy infiltrates, and immune stromal ring; and (b) 5 months later showing resolution with residual corneal scar.



(Figure 4). The patient was advised to continue oral acyclovir 400 mg once daily for 1 year and has shown no recurrences since.

Discussion

A series of 6 patients with HSV-1 endotheliitis with progressive manifestations has been described. The first 2 patients were initially diagnosed with bacterial keratitis. A differential diagnosis of endophthalmitis was ruled out by serial B-scan ultrasonography. Viral aetiology was established only after penetrating keratoplasty, when corneal tissue was found to be positive for viral DNA. This aetiological confirmation helped to diagnose the last 4 consecutive patients, who had similar clinical presentations. It was thus possible to institute prompt treatment, resulting in better clinical outcomes than for the first 2 patients.

Until recently, HSV endotheliitis was a poorly understood entity. Various studies have implicated HSV as the aetiological agent and the virus, its antigen, and its DNA have all been isolated from corneal endothelial cells, consistent with the inflammatory as well as infective nature of this disease.[5-8] Prior to the development of sensitive identification techniques such as PCR, the aetiology of many cases of presumed viral endotheliitis remained conjectural. In addition, with diagnosis based solely on clinical features, the viral aetiology, especially in progressive presentations, would have been completely unsuspected and overlooked.

PCR has proved to be an extremely useful tool for the diagnosis of difficult conditions using a variety of ocular specimens. Kaye et al have reported the sensitivity of PCR for detection of HSV-1 DNA in HSV keratitis as 82%, and a combination of PCR and immunohistochemistry increased the sensitivity to 97%.[9] In the present series, PCR was performed on 11 samples from 8 eyes and was positive in 6 samples from 4 eyes. Negative results may have been due to the presence of PCR inhibitors or a low viral load in those specimens. Due to the retrospective nature of the series, specimens were not spiked with known viral DNA to rule out the presence of inhibitors. Casual positivity of PCR can be ruled out because multiple specimens from the same eye (for example, aqueous fluid plus corneal button from patient 2 and corneal scrapings plus aqueous fluid from patient 6) were positive for HSV-1 DNA.

Typically, HSV endotheliitis has been described as unilateral stromal oedema, with underlying keratic precipitates and mild anterior chamber reaction.[2,3] Progression to immune stromal keratitis was found only in severe cases or in persistent oedema. Occasionally, HSV endotheliitis may present atypically in a milder form.[10] In contrast, in the present series, all patients presented with severe disease at the onset, with bilateral involvement in 4 of 6 patients. In addition, epithelial involvement, stromal infiltrates, endothelial exudates, and severe anterior chamber reaction were observed at the acute stage. Generally, these findings are not expected in classical HSV endotheliitis. However, progressive HSV endotheliitis may be associated with dendritic ulceration, disciform oedema, marked elevation in intraocular pressure, and uveitis.[11]

Epithelial involvement was encountered in 4 eyes in this series. The mechanism for epithelial breakdown may be multifactorial, including drug toxicity, metaherpetic keratitis, or even direct epithelial invasion by live virus reactivated in the trigeminal ganglion and shed into tears. In patients 2 and 6, scrapings from the corneal epithelium were PCR-positive for viral DNA, suggesting the possibility of concurrent viral invasion of the epithelium. Stromal infiltrates, as seen in 3 eyes, may have been due to inflammatory spillover from the endothelium. Other progressive features seen

in the patients in this series were endothelial exudates (3 eyes), Wesseley's type immune ring (1 eye), and hypopyon (5 eyes). These features may correlate positively with the severity of inflammation.

This study suggests that the spectrum of viral endotheliitis may be broader than defined in the literature. O'Brien et al have suggested the following 2 factors as possible sources of variation in the clinical spectrum of symptoms: patient factors such as geographical differences, subtle changes in the immune status of the host, and genetic and racial predisposition, and viral factors, such as the type of viral isolate (whether a more virulent strain) and viral dose.[12] Some of these factors may be responsible for the variations between patients described in this report.

In summary, progressive manifestations in the form of epithelial defects, stromal infiltrates, and severe anterior chamber reaction can occur in HSV endotheliitis. Thus, delay in diagnosis and treatment may lead to sight-threatening complications. Detection of HSV-1 DNA by PCR is helpful but negative results do not exclude a viral aetiology. Recognising a clinical profile as similar to that of the patients described here may help to achieve an early diagnosis and allow appropriate therapy to be instituted promptly.

References

1. Hendricks RL. An immunologist's view of herpes simplex keratitis: Thygeson Lecture 1996, presented at the Ocular Microbiology and Immunology Group meeting, October 26, 1996. Cornea. 1997;16: 503-6.
2. Liesegang TJ. Herpes simplex virus epidemiology and ocular importance. Cornea. 2001;20:1-13.
3. Holland EJ, Schwartz GS. Classification of herpes simplex virus keratitis. Cornea. 1999;18:144-54.
4. Aurelius E, Johansson B, Skoldenberg B, et al. Rapid diagnosis of herpes simplex encephalitis by nested polymerase chain reaction assay of cerebrospinal fluid. Lancet. 1991;337;189-92.
5. Pepose JS. Herpes simplex keratitis: role of viral infection versus immune response. Surv Ophthalmol. 1991;35:345-52.
6. Ohashi Y, Yamamoto S, Nishida K, et al. Demonstration of herpes simplex virus DNA in idiopathic corneal endotheliopathy. Am J Ophthalmol. 1991;112:419-23.
7. Holbach LM, Asano N, Naumann GO. Infection of the corneal endothelium in herpes simplex keratitis. Am J Ophthalmol. 1998;126:592-4.
8. Zheng X, Yamaguchi M, Goto T, et al. Experimental corneal endotheliitis in rabbit. Invest Ophthalmol Vis Sci. 2000;41:377-85.
9. Kaye SB, Baker K, Bonshek R, et al. Human herpesviruses in the cornea. Br J Ophthalmol. 2000;84:563-71.
10. Bass SJ, Sherman J, Panariello G, et al. Atypical herpetic endotheliitis. J Am Optom Assoc. 1995;66:577-80.
11. Robin JB, Stergner JB, Kaufman HE. Progressive herpetic corneal endotheliitis. Am J Ophthalmol. 1985;100:336-7.
12. O'Brien WJ, Guy J, Taylor JL. Pathogenesis of corneal oedema associated with herpetic eye disease. Br J Ophthalmol. 1990;74:723-30.

Correlation between Histopathology and Ultrasound Biomicroscopy of Uveal Tumours

Sujata Guha, Jyotirmoy Biswas, Krishnakumar Subramanian, Tarun Sharma, Mahesh P Shanmugam
Sankara Nethralaya, Vision Research Foundation, Chennai, India

Aim: *To retrospectively assess correlations between features of anterior segment tumours revealed by ultrasound biomicroscopy and histopathological findings.*
Methods: *The records of 8 patients who underwent enucleation for uveal melanoma (6 eyes) or uveal metastasis (2 eyes) were reviewed. Preoperative ultrasound biomicroscopy and histopathological features were compared with respect to tumour margins, internal reflectivity, supraciliary effusion, and scleral involvement.*
Results: *Good correlation was observed with respect to tumour margin (7 eyes), scleral involvement (8 eyes), internal reflectivity and tissue characteristics (7 eyes), and supraciliary effusion (6 eyes).*
Conclusions: *Ultrasound biomicroscopy is a valuable, non-invasive tool for assessing anterior segment tumours in vivo.*

Key words: *Eye neoplasms, Pathology, Retrospective study, Ultrasound biomicroscopy, Uvea*

Asian J Ophthalmol. 2007;9:82-6

Introduction

The diagnosis of peripheral choroidal and ciliary body melanoma may sometimes be difficult because of its anterior location.[1] With conventional ultrasound (10 MHz), it may not always be possible to image the anterior extent of a peripherally located uveal melanoma and resolution is poor.[2-5] However, ultrasound biomicroscopy (UBM), with its high frequency (50 MHz) and high resolution can delineate the anterior extent, reflectivity pattern, and intrascleral invasion or extrascleral extension.[3-6]

In this study of patients who required enucleation for anterior uveal tumour, the correlation between UBM and histopathological features was assessed with respect to tumour margin, internal reflectivity, supraciliary effusion, and extrascleral extension.

Methods

Eight patients, 6 men and 2 women, were included in this study. The average age was 45 years (range, 15 to 74 years). In each patient, enucleation was necessary because of an anterior uveal tumour. Patient records were reviewed retrospectively.

Correspondence: Dr Sujata Guha, Sankara Nethralaya, 18 College Road, Chennai 600 017, Tamil Nadu, India.
Tel: (91 044) 2827 1616; Fax: (91 044) 2825 4180;
E-mail: drsg@sankaranethralaya.org

Ultrasound Biomicroscopy

Prior to surgery, all eyes were examined with an ultrasound biomicroscope (Model 840, Humphrey-Zeiss, San Leandro, USA) using a 50 MHz probe, which provides a resolution of 50 mm and a tissue penetration depth of 4 to 5 mm. A polymethyl methacrylate eyecup of a suitable size was inserted between the eyelids to keep them open and facilitate the use of a coupling solution (methylcellulose). The various structures and meridians were scanned by asking the patient to move the eye in different directions; the probe was always placed perpendicular to the structure to be scanned. Generated images were recorded on an optical disc recorder. The time required per patient was approximately 10 minutes and patients tolerated the procedure well.

Histopathological Assessment

Enucleated specimens were fixed in 10% neutral buffered formalin and embedded in paraffin. Multiple 6 mm sections were stained with haematoxylin and eosin and viewed under the light microscope.

Results

Findings for all patients are summarised in Table 1. Of the 8 patients examined, 6 had uveal melanomas (1 ciliary body, 2 ciliochoroidal, and 3 choroidal), 1 had ciliary body metastasis from toe melanoma, and 1 had metastasis to the iris and ciliary body from a lung

Table 1. Correlation between ultrasound biomicroscopy and histopathology.

Patient number	Age (years)/sex	Diagnosis	Extent*		Scleral extension		Supraciliary effusion		Acoustic pattern and tissue characteristics	
			UBM	HPE	UBM	HPE	UBM	HPE	UBM	HPE
1	45/M	Choroidal melanoma	CB (-)	CB (-)	No	No	Yes	Yes	Moderately reflective, few cystic spaces	Moderately packed, vascular channels, spindle cells
2	63/M	Ciliochoroidal melanoma	CB (+), posterior only	CB (+), posterior only	No	No	Yes	Yes	Low reflectivity, uniform	Tightly packed, mixed cells
3	50/M	Choroidal melanoma	CB (-)	CB (-)	No	No	Yes	Yes	Variable reflectivity, cystic spaces	Tightly packed, vascular channels, spindle cells
4	45/F	CB metastasis	CH (-)	CH (-)	No	No	No	No	Moderately reflective	Packed clumps of metastatic cells
5	30/F	CB and iris secondaries	CH (-)	CH (-)	No	No	No	No	Moderately reflective, cystic spaces	Tightly packed, vascular channels
6	42/M	Ciliochoroidal melanoma	CB tumour, CH (+)	CB tumour, CH (+)	No	No	No	Yes	Low reflectivity, uniform	Tightly packed, mixed cells
7	74/M	Ciliary body melanoma	CH (+)	CH (-)	No	No	Yes	Yes	Moderately reflective	Moderately packed, spindle cells
8	15/M	Choroidal melanoma	CB (-)	CB (-)	No	No	No	Yes	Tumour not imaged	Loosely packed, vascular channels, mixed cells

* (+) or (-) indicates involvement or lack of involvement of the specified tissue.
Abbreviations: CB = ciliary body; CH = choroid; HPE = histopathological examination; UBM = ultrasound biomicroscopy.

carcinoid tumour. The following are detailed descriptions of 6 representative patients.

Patient 1 was a 45-year-old man whose left fundus showed a peripheral choroidal tumour and associated vitreous haemorrhage. UBM showed a peripheral choroidal mass without any ciliary body involvement as a moderately reflective lesion with few cystic spaces and supraciliary effusion (Figures 1a and b). Histopathological evaluation confirmed that the lesion was choroidal melanoma sparing the ciliary body. The melanoma was of a moderately packed spindle-cell type with vascular channels. The latter appear to correspond to hypoechoic regions located by UBM. A space between the sclera and choroid was also noted (Figure 1c). No scleral extension was evident by UBM or histopathology.

For patient 2, a 63-year-old man, UBM showed a ciliochoroidal mass with no ciliary process involvement in the right eye. The mass was homogenous with low to moderate internal reflectivity and highly reflective echoes near the scleral surface (Figure 2a). There was an echolucent space between the ciliary body and sclera and the overlying sclera was normal. Histopathology showed a mass arising from the anterior part of the choroid spilling over to the ciliary body. However, the anterior ciliary body was spared. The mass was composed of tightly packed cells (Figure 2b) corresponding to low reflectivity by UBM. Supraciliary effusion was present and no scleral extension was observed.

In patient 3, a 50-year-old man, UBM showed a homogenous mass with low to moderate reflectivity arising from the choroid

Figure 1. Patient 1. (a) Ultrasound biomicroscopy photograph showing a peripheral choroidal mass located behind the ciliary body — echolucent spaces correspond to vascular channels (red arrow) and choroidal stripping is seen as an echolucent space between the choroid and the sclera (white arrow); (b) ultrasound biomicroscopy photograph showing low to moderate reflective echoes in the choroid with echolucent spaces corresponding to vascular channels (red arrow) and choroidal stripping (white arrow); and (c) photomicrograph showing pigmented choroidal tumour with vascular channels randomly placed (arrows) [haematoxylin and eosin stain; original magnification, x 150].

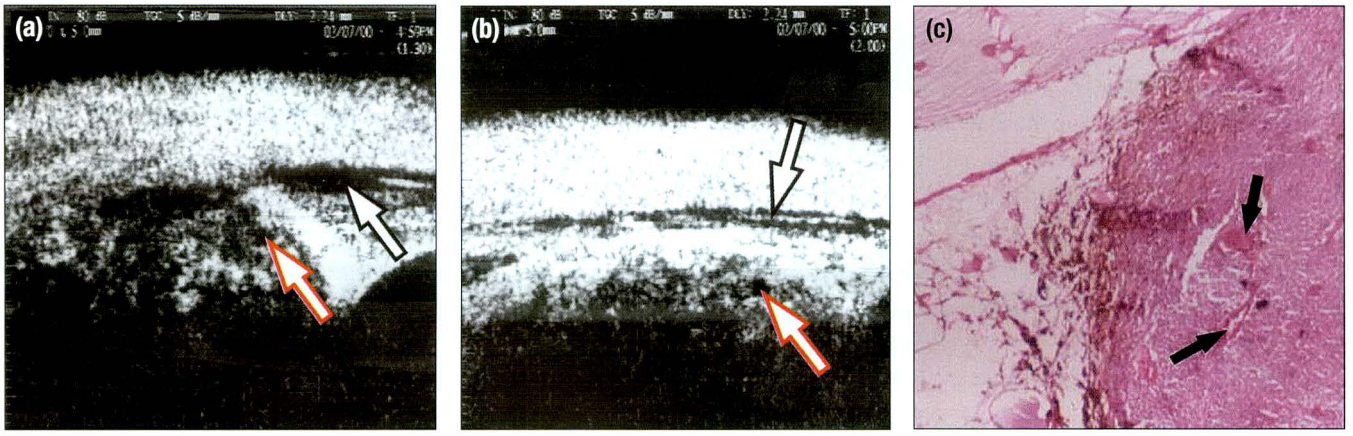
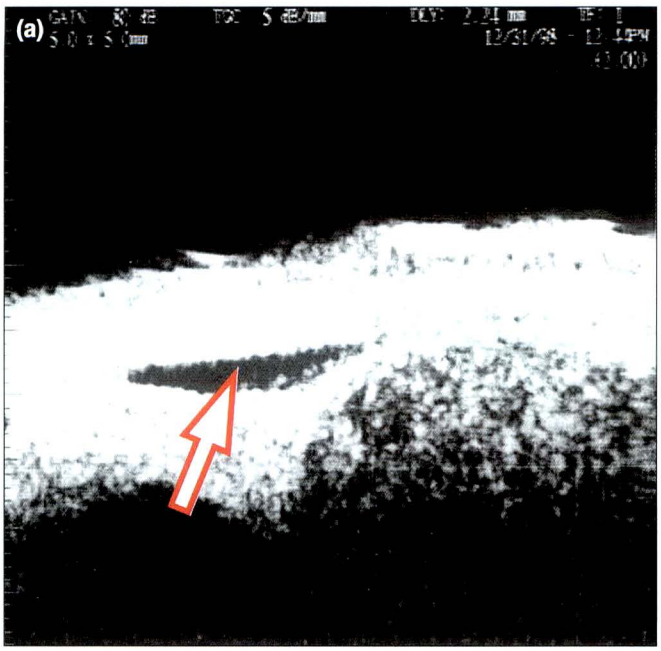


Figure 2. Patient 2. (a) Ultrasound biomicroscopy photograph showing low to moderate internal echoes with high reflective echo near the scleral surface — a triangular space between the sclera and the choroid is also seen (red arrow) representing choroidal stripping; and (b) photomicrograph showing cilio-choroidal melanoma with tightly packed tumour cells — the choroid is separated from the sclera (arrow) [haematoxylin and eosin stain; original magnification, x 100].



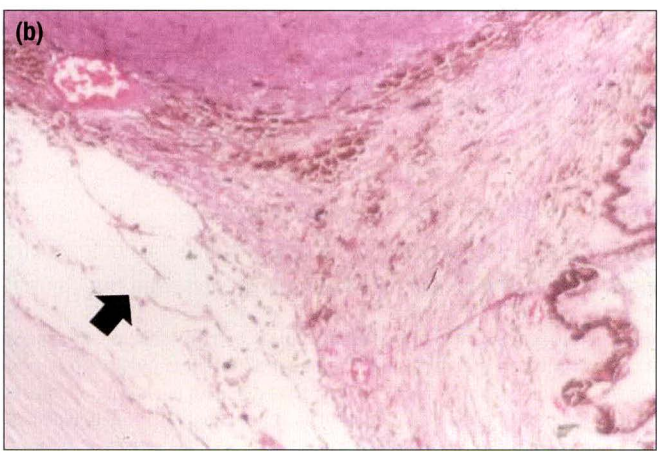
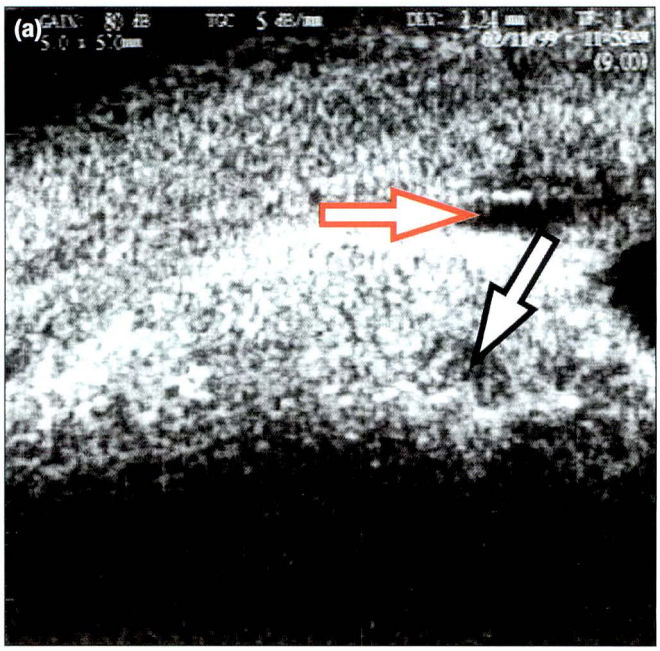
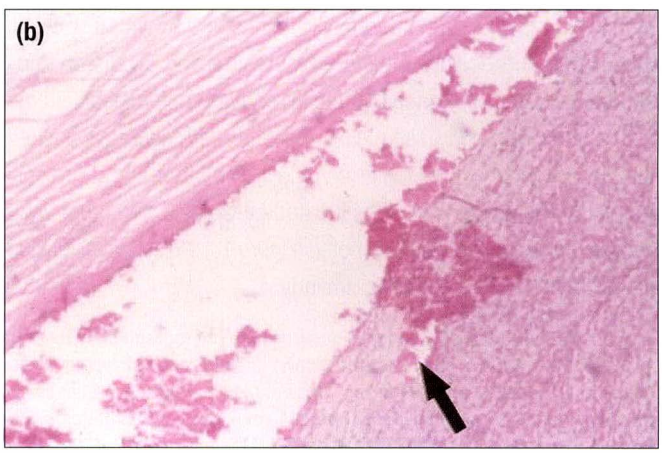


Figure 3. Patient 3. (a) Ultrasound biomicroscopy photograph showing moderate reflective homogenous echoes in the choroid with a large hypoechoic space (white arrow), which correlates with vascular channels seen on histopathology — choroidal stripping (red arrow) is also seen; and (b) photomicrograph of choroidal melanoma showing tightly packed spindle cells with randomly oriented vessels (arrow) [haematoxylin and eosin stain; original magnification, x 100].



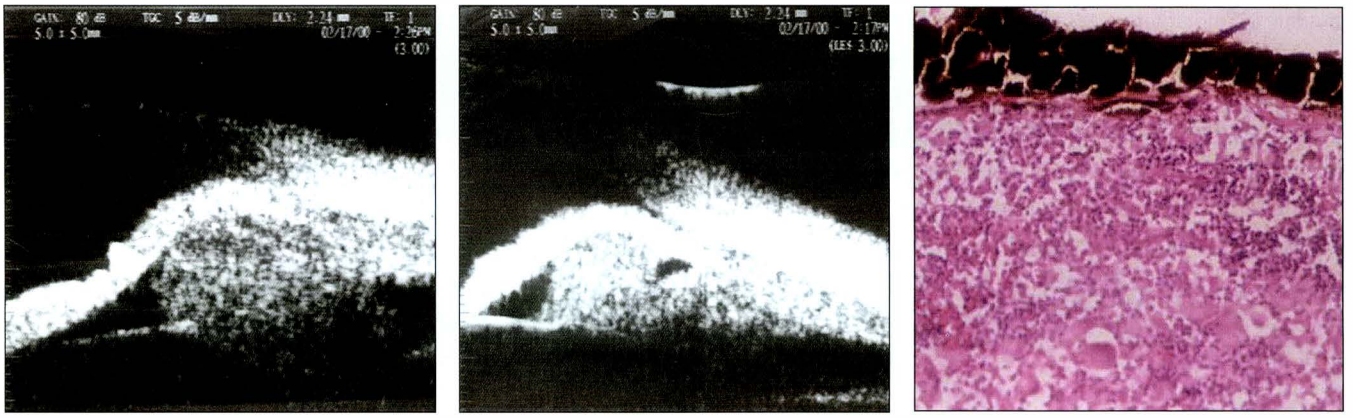


with no ciliary body involvement (Figure 3a). The mass had several echolucent spaces. Supraciliary effusion was present with no scleral extension. Histologically, the melanoma showed tightly packed spindle cells with vascular channels and no ciliary body involvement (Figure 3b). Supraciliary effusion was present and no scleral extension was observed.

Patient 4, a 45-year-old woman with a history of excision of toe melanoma 15 years previously, was observed to have a retrolenticular mass. Ophthalmoscopy showed vitreous haemorrhage and a few pigment clumps. UBM showed moderate reflective echoes on the undersurface of the iris and ciliary body spilling onto the vitreous (Figures 4a and b). This was corroborated by histopathology. There was no evidence of supraciliary effusion or scleral extension either on UBM or histopathology (Figure 4c).

Patient 5, a 30-year-old woman, presented with a retro-iridial mass causing indentation of the lens. Another creamish-yellow lesion was present at the posterior choroid. She had undergone excision of a lung tumour previously. UBM showed variably reflective lesions in the retro-iridial mass with hypoechoic areas (Figures 5a and b). The peripheral choroid was not involved. Histopathologic examination revealed tightly packed tumour cells with numerous vascular channels (Figure 5c), corresponding with low reflectivity

Figure 4. Patient 4. (a) Ultrasound biomicroscopy photograph showing moderate reflective echoes on the under surface of the iris and ciliary sulcus; (b) ultrasound biomicroscopy photograph showing moderate reflective echoes on the under surface of the iris — small hypoechoic spaces are seen in between signifying cell clumps; and (c) photomicrograph showing tumour nodule attached to the pigmented epithelium of ciliary body — the tumour cells are loosely arranged with dense collections of lymphocytes (haematoxylin and eosin stain; original magnification, x 100).



cystic spaces detected by UBM. There was no involvement of the peripheral choroid or sclera. Pathological diagnosis was carcinoid tumour metastasis to the ciliary body and choroid.

Patient 7, a 74-year-old man, presented with a retro-irideal mass with haemorrhagic spots on the surface. UBM showed a ciliary body mass involving the peripheral choroid and angle. The lesion was moderately reflective with uniform echogenicity. Ciliary body stripping was observed at the margin. The posterior extent of the tumour could not be ascertained by UBM. Histopathology confirmed ciliary body melanoma of a moderately packed spindle-cell type, which did not extend into the choroid. The sclera was normal but supraciliary effusion was evident.

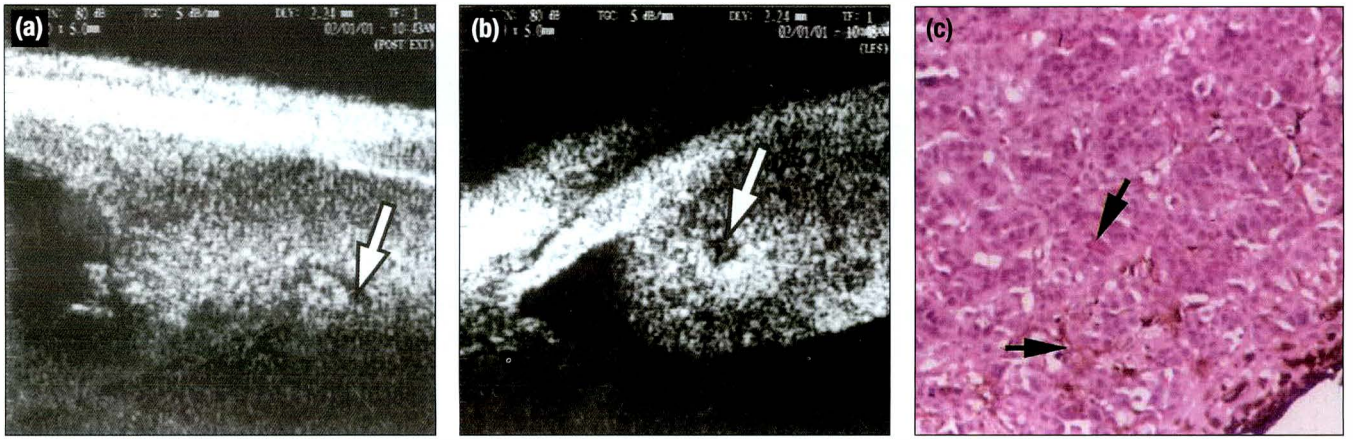
Extent of Tumour

In 7 of the 8 patients, UBM and histopathology correlated well with respect to the anterior extent of the tumour (Table 1): 3 cases of choroidal melanoma did not show any extension into the ciliary body (patients 1, 3, and 8), 2 cases of ciliochoroidal melanoma involved the posterior ciliary body and the peripheral choroid only (patients 2 and 6), 1 case of ciliary body metastasis did not involve the choroid (patient 4), and 1 case of ciliary body and iris metastasis did not show involvement of the anterior choroid (patient 5). In one case (patient 7), a ciliary body melanoma, UBM showed choroidal involvement but histopathology did not show this.

Scleral Extension and Supraciliary Effusion

Histopathology did not show intrascleral invasion in any of the 8 patients and this finding was supported by UBM. In 6 cases (patients 1 to 5 and 7), UBM and histopathology were in agreement about the presence or absence of supraciliary effusion. In the remaining 2 cases, effusion was not evident in UBM images but was detected by histopathology.

Figure 5. Patient 5. (a) Ultrasound biomicroscopy photograph showing low to moderate reflective echoes in the ciliary body region with few hypoechoic areas (arrow) representing vascular channels; (b) ultrasound biomicroscopy photograph showing low to moderate reflective echoes on the under surface of the iris with plenty of hypoechoic areas (arrow) representing vascular channels; and (c) photomicrograph showing ciliary body mass comprising tumour cells arranged in small nest-like pattern — the lobules are separated by fibrous septae and a few scattered vascular channels (arrows) are seen (haematoxylin and eosin stain; original magnification, x 100).



Acoustic Pattern and Tissue Characteristics

In 2 cases (patients 2 and 6), low reflectivity on UBM was associated with tightly packed mixed cells; in 4 cases (patients 1, 4, 5, and 7), moderate reflectivity was associated with moderate to tightly packed cells, and in 1 case (patient 3) reflectivity was variable and histopathology revealed the presence of vascular channels. In 3 cases (patients 1, 3, and 5), cystic spaces appearing as echolucent spaces in UBM images were associated with the presence of vascular channels by histopathology. However, there was no overall consistent correlation between the reflectivity pattern obtained by UBM and the type(s) of cells indicated by histopathology.

Discussion

Unlike posterior choroidal melanoma, ciliochoroidal melanomas are difficult to visualise and the anterior extent of the tumour cannot be precisely known.[1,4,5] Although transillumination does help in delineating the tumour extent, it is dependent on tumour characteristics such as melanin pigment or haemorrhage. Conventional ultrasound cannot image the ciliary body area well and lacks sufficient resolution.[2-5] In such clinical situations, high-frequency UBM provides high-resolution cross-sectional images of the involved areas, which highlight very precisely the anterior extent of the tumour, scleral involvement, supraciliary effusion, and internal reflectivity.[3-6] The additional information that UBM provides may be helpful when choosing between various treatment options: tumour resection, brachytherapy, or enucleation.

In this study, in all but one patient, the extent of the tumour as defined by UBM correlated well with the histopathological assessment. Similarly, both methods were in agreement about scleral involvement and there were some apparent correlations between acoustic patterns and tissue characteristics. Tightly packed tumour cells, which provide less acoustic interfaces, exhibited low ultrasound reflectivity. Similarly, vascular channels identified histologically appeared as echolucent areas in UBM images. However, UBM could not differentiate between spindle-cell type and mixed-cell type tumours. The presence of uveal tissue stripping detected as supraciliary effusion by UBM was observed histopathologically in most patients. It should be noted that the retrospective nature of this study represents a possible source of bias. Re-examining the UBM images after looking at the histopathology results may have introduced findings overlooked at first examination.

There are few reports of studies in which UBM and histopathological features of anterior uveal tumours have been compared.[4,7] In a study of 3 patients with ciliary body melanoma by Marigo et al, UBM images correlated well with histopathological features of anterior uveal melanomas, including shape, reflectivity, and local extension.[4] Maberly et al also reported UBM to be a reliable imaging technique for the evaluation of the anterior aspect of peripheral choroidal melanomas.[5] In the latter study, there was agreement between UBM and histopathology of ciliochoroidal effusion at the leading edge of the tumour, which occurred in melanomas involving the pars plana region but not in those involving the pars plicata, iris root, or angle structures.[5] In the present study, none of the patients with melanoma involved the pars plicata or the area anterior to it.

One of the prognostic factors for uveal melanoma is the vascular pattern and several patterns have been demonstrated.[8] In the present study, cystic spaces in UBM images were consistently associated with the presence of a vascular pattern in this study, indicating a need for further investigation to verify this apparent correlation and establish its relationship with mortality. At present, this issue should be regarded as speculative since cystic spaces may represent either vascular channels or variations in cellular composition.

This study demonstrates that UBM is a reliable imaging technique for assessing ciliochoroidal tumours in vivo and that it compares well with histopathological findings.

Acknowledgements

Supported by the Vision Research Foundation, Chennai, India. Presented in part as a scientific poster at the 2002 Annual Meeting of the American Academy of Ophthalmology, Orlando, Florida, USA.

References

1. McLean IW, Foster WD, Zimmerman LE. Prognostic factors in small malignant melanomas of the choroid and ciliary body. Arch Ophthalmol. 1977;95:48-58.
2. Coleman DJ, Silverman R, Rondeau MJ, et al. Correlations of acoustic tissue typing of malignant melanoma and histopathologic features as a predictor of death. Am J Ophthalmol. 1990;110:380-8.
3. Pavlin CJ, Harasiewicz K, Eng P, et al. Ultrasound biomicroscopy of anterior segment structures in normal and glaucomatous eyes. Am J Ophthalmol. 1992;113:381-9.
4. Marigo FA, Finger PT, McCormick SA, et al. Iris and ciliary body melanomas: ultrasound biomicroscopy with histopathologic correlation. Arch Ophthalmol. 2000;118:1515-21.
5. Maberly DA, Pavlin CJ, McGowan HD, et al. Ultrasound biomicroscopic imaging of the anterior aspect of peripheral choroidal melanomas. Am J Ophthalmol. 1997;123:506-14.
6. Pavlin CJ, McWhae JA, McGowan HD, et al. Ultrasound biomicroscopy of anterior segment tumors. Ophthalmology. 1992;99:1220-8.
7. Marigo FA, Finger PT, McCormick SA, et al. Anterior segment implantation cysts: ultrasound biomicroscopy with histopathologic correlation. Arch Ophthalmol. 1998;116:1569-78.
8. Rummelt V, Folberg R, Woolson RF, et al. Relation between the microcirculation architecture and the aggressive behavior of ciliary body melanomas. Ophthalmology. 1995;102:844-51.

Bilateral Acute Angle Closure Glaucoma following Administration of Oral Pseudoephedrine for Sinusitis

Rohit Sharma, Andrew Waldock
Eye Unit, Luton & Dunstable NHS Trust, Luton, UK

This report is of a patient with bilateral simultaneous angle closure glaucoma induced by oral pseudoephedrine administered for sinusitis. A 62-year-old woman presented with features of bilateral acute angle closure. She had been using oral Sinutab (pseudoephedrine and paracetamol) for sinusitis for 3 days prior to presentation and drug-induced glaucoma was diagnosed.

Key words: *Ephedrine, Glaucoma, angle closure, Sinusitis*

Asian J Ophthalmol. 2007;9:87-8

Introduction

Bilateral simultaneous angle closure glaucoma (ACG) has been described before,[1-7] but is a rare entity. The postulated mechanism for drug-induced bilateral acute angle closure is ciliochoroidal detachment, swollen ciliary processes, and a forward shift of the lens.[8,9] Several classes of drugs, including adrenergic agonists, cholinergics, anticholinergics, selective serotonin reuptake inhibitors, antidepressants, anticoagulants, and antihistamines, have been reported to induce or precipitate acute angle closure glaucoma (AACG).[1]

This report is of a patient with bilateral simultaneous ACG induced by oral pseudoephedrine used for sinusitis treatment. This phenomenon has not been reported in the literature before.

Case Report

A 62-year-old Caucasian woman presented to the Eye Casualty of Luton and Dunstable Hospital, Luton, UK, in September 2006 with worsening bilateral eye pain, watering, and photophobia for 7 days, and decreased vision and nausea for 3 days. Her past ocular history was unremarkable, with no family history of glaucoma. There was no medical history of hypertension, diabetes, heart disease, or asthma.

A recent medical history revealed that she had been taking oral Sinutab 4 times daily for 3 days prior to developing eye symptoms. Sinutab consists of paracetamol 500 mg and pseudoephedrine hydrochloride 30 mg per tablet and is available over-the-counter as a non-sedating treatment for sinusitis. She was not taking any other medication at the time.

Examination revealed visual acuity of 6/60 in the right eye and 6/24 in the left eye, with bilateral corneal stromal oedema. Both anterior chambers were shallow with 2+ flare and cells. Her intraocular pressures (IOPs) were 66 mm Hg in the right eye and 60 mm Hg in the left eye. She was given intravenous acetazolamide 500 mg once, followed by pilocarpine 2%, timolol 0.5%, and prednisolone 0.5% eye drops. After 2 hours, she had significant relief of symptoms with IOPs of 24 mm Hg in the right eye and 22 mm Hg in the left eye. She was advised to discontinue the oral medication for sinusitis. At gonioscopy, the right eye showed no angle structures and the left eye showed anterior trabeculum in the inferior 90° and no angle structures in the remaining 270°. The refraction was +2.00/0.50-60, near add +2.25 in the right eye and +2.25, near add +2.25 in the left eye. Bilateral YAG laser peripheral iridotomy was performed 2 days later. She has since maintained normal IOPs and healthy discs with no further medication.

Discussion

AACG is a known side effect of sympathomimetics.[1,2] Pseudoephedrine is found in many over-the-counter preparations, either as single-ingredient preparations or, more commonly, in combination medicines. Although the product information leaflet mentions glaucoma as a contraindication or as an adverse effect, the symptoms and type of glaucoma are not specified. The warning signs of glaucoma need to be mentioned clearly on the product leaflet. The possibility of drug-induced glaucoma should be kept in mind by medical practitioners. Immediate discontinuation of the medicine and referral to an ophthalmologist is required.

Correspondence: Dr Rohit Sharma, 14 Calnwood Road, Luton LU4 0ET, UK.
Tel: (44 783) 819 5313;
E-mail: rohity2ksharma@yahoo.com

References

1. Tripathi RC, Tripathi BJ, Haggerty C. Drug-induced glaucomas: mechanism and management. Drug Saf. 2003;26:749-67.
2. Khan MA, Watt LL, Hugkulstone CE. Bilateral acute angle-closure glaucoma after use of Fenox nasal drops. Eye. 2002;16:662-3.
3. Srinivasan R, Kaliaperumal S, Dutta TK. Bilateral angle closure glaucoma following snake bite. J Assoc Physicians India. 2005;53:46-8.
4. Ezra DG, Storoni M, Whitefield LA. Simultaneous bilateral acute angle closure glaucoma following venlafaxine treatment. Eye. 2006;20: 128-9.
5. Zelefsky JR, Fine HF, Rubinstein VJ, et al. Escitalopram-induced uveal effusions and bilateral angle closure glaucoma. Am J Ophthalmol. 2006; 141:1144-7.
6. Kirwan JF, Subak-Sharpe I, Teimory M. Bilateral acute angle closure glaucoma after administration of paroxetine. Br J Ophthalmol. 1998; 82:976-8.
7. Tapie R. Acute bilateral glaucoma following the instillation of a 5% neosynephrine eyewash. Bull Soc Fr Dermatol Syphiligr. 1957;64: 691-3.
8. Levy J, Yagev R, Petrova A, et al. Topiramate-induced bilateral angle-closure glaucoma. Can J Ophthalmol. 2006;41:221-5.
9. Postel EA, Assalian A, Epstein DL. Drug-induced transient myopia and angle-closure glaucoma associated with supraciliary choroidal effusion. Am J Ophthalmol. 1996;122:110-2.

Sympathetic Ophthalmitis following Therapeutic Penetrating Keratoplasty

Sejal Maheshwari, Vinita Rao
Cornea and Refractive Services, Shri Ganapati Netralaya, Jalna, India

This report is of a patient with presumed sympathetic ophthalmia following therapeutic penetrating keratoplasty. Therapeutic penetrating keratoplasty with subsequent inflammation should be viewed as a possible inciting agent for sympathetic ophthalmia and surgeons should be alert to this possibility in the event of visual complaints in the better eye.

Key words: *Differential diagnosis, Penetrating keratoplasty, Sympathetic ophthalmia*

Asian J Ophthalmol. 2007;9:89-91

Introduction

Sympathetic ophthalmia is a bilateral diffuse granulomatous uveitis occurring in patients who have sustained previous ocular injury, either as a result of trauma or as a rare consequence of ocular surgery. The incidence of sympathetic ophthalmia after a routine surgical procedure has been estimated to be approximately 1 in 10,000 patients treated.[1]

Ophthalmic surgical procedures that have been reported to result in sympathetic ophthalmia include cataract surgery, glaucoma filtering surgery, scleral buckling, pars plana vitrectomy, laser cyclophotocoagulation, and proton beam irradiation.[2] This appears to be the first report of a patient in which sympathetic ophthalmia occurred following therapeutic penetrating keratoplasty.

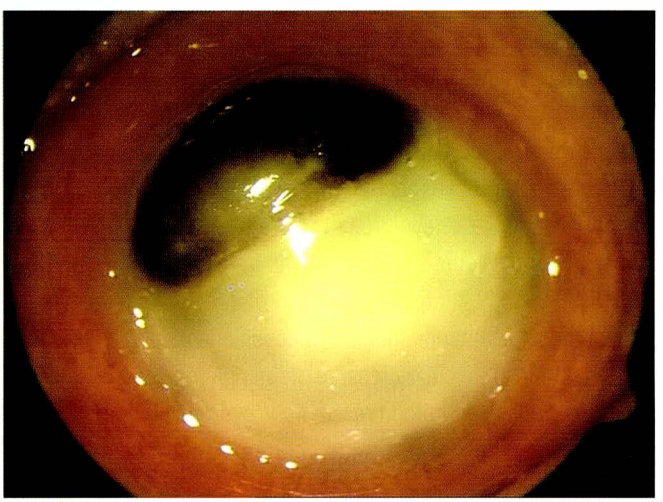
Case Report

A 30-year-old woman was referred to the authors for a non-healing fungal corneal ulcer in the left eye. She had sustained blunt trauma to the left eye caused by vegetative matter approximately 1 month previously and had decreased vision and redness and pain in the affected eye since then. Microbiological evaluation by the primary ophthalmologist revealed unidentified fungal growth on culture. She was treated with topical antifungals and antibiotics.

At examination, visual acuity was 6/6, N6, in the right eye and perception of light with defective projection of rays in the left eye. Slit-lamp examination of the left eye revealed total corneal infiltrate. The intraocular pressure of the left eye was raised. Ultrasonography of the left eye was within normal limits. Treatment with oral ketoconazole 200 mg twice daily and acetazolamide 250 mg 3 times daily was started and the following eye drops were given: ketaconazole 4%, natamycin 5%, amphotericin B 0.15%, and ofloxacin 3%, all half hourly, and atropine 1% 3 times daily. The patient was followed up weekly and developed corneal melt in the superonasal quadrant with iris prolapse after 2 weeks (Figure 1). Ultrasonography revealed a clear vitreous cavity with choroidal detachment. At this stage, therapeutic penetrating keratoplasty was undertaken, infected corneal tissue was excised, exudates noted on the lens and iris were removed, an intracameral amphotericin B wash was performed, and a donor cornea 11 mm in diameter was sutured with 16 interrupted 10.0 nylon sutures.

In the early postoperative period, the graft was oedematous, and grade 4+ anterior chamber cells were present (Figure 2). Treatment was oral prednisolone 1 mg/kg body weight daily, tapered gradually over a period of 1 month, and natamycin 5%

Figure 1. Perforated corneal ulcer in the left eye.



Correspondence: Dr Sejal Maheshwari, Cornea and Refractive Services, Shri Ganapati Netralaya, Jalna 431 203, India.
Tel: (91 248) 223 9001;
E-mail: sejalm@netralaya.org

Figure 2. One day after therapeutic penetrating keratoplasty.

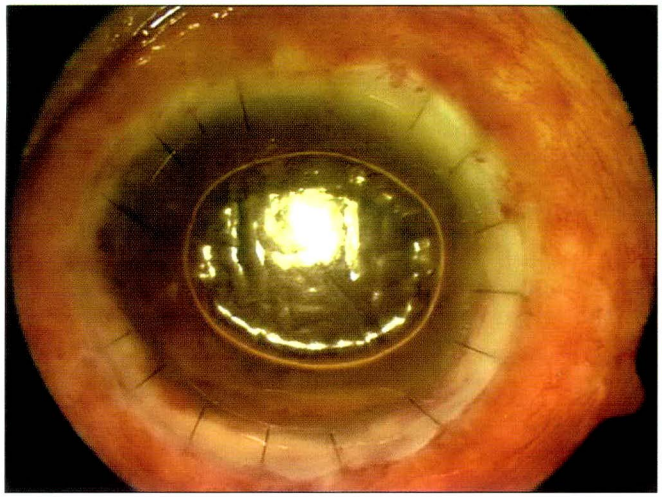
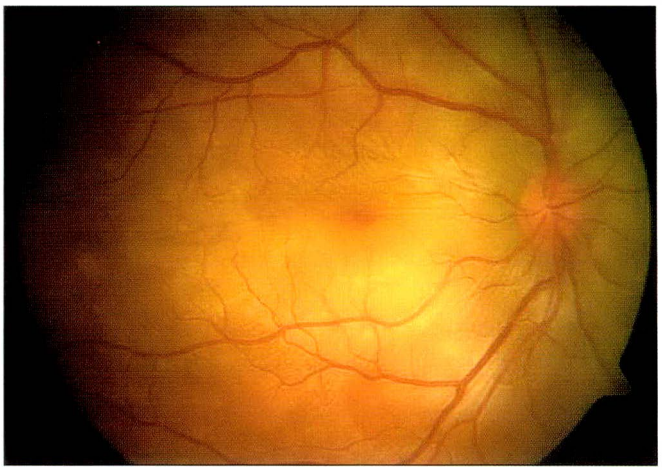


Figure 3. Inferior exudative retinal detachment with choroidal infiltrates in the right eye 2 months after surgery.



and ofloxacin 3% eye drops every 2 hours. One month after therapeutic penetrating keratoplasty, visual acuity in the left eye was perception of light with defective projection of rays and examination showed graft oedema with resolution of anterior chamber inflammation. Visual acuity in the right eye was 6/6, N6, and anterior segment examination was unremarkable.

Two months after surgery, the patient complained of blurring of vision in the right eye for approximately 2 weeks and vision in the left eye remained poor. The corrected visual acuity, with a +2.0 D sphere, was 6/6, N6, in the right eye. Slit-lamp examination of the right eye revealed circumciliary congestion, keratic precipitates in the inferior half of the cornea, grade 1+ anterior chamber cells, and flare in the anterior chamber. Examination of the left eye revealed circumciliary congestion and graft oedema with keratic precipitates in the inferior half of the cornea. Intraocular pressure was 38 mm Hg in the right eye. Dilated fundus examination of the right eye revealed grade 1+ vitritis and exudative retinal detachment involving the inferior half with multiple yellow-white choroidal infiltrates (Figure 3).

Ultrasonography of the right eye did not reveal any scleral or choroidal thickening. There was no view of the fundus in the left eye. A diagnosis of sympathetic ophthalmia was made and the patient was treated with oral prednisolone 1 mg/kg body weight daily in tapering doses, acetazolamide 250 mg once a day, and timolol maleate 0.5% eye drops twice daily in the right eye.

Two months later, uncorrected visual acuity in the right eye was 6/6, N6. Slit-lamp examination of the right eye revealed resolution of the anterior chamber reaction and the left eye showed phthisis bulbi. Intraocular pressure of the right eye was 14 mm Hg. Dilated fundus examination of the right eye revealed an attached retina and disappearance of the choroidal infiltrates. A tapering dose of oral prednisolone was continued.

Discussion

Sympathetic ophthalmia has been reported to occur mainly after trauma. However, it has also been reported following corneal perforation with uveal prolapse and ocular surgery such as cataract surgery, glaucoma filtering surgery, scleral buckling, pars plana vitrectomy, laser cyclophotocoagulation, or proton beam irradiation.[2-7] This report is of a patient with presumed sympathetic ophthalmia incited by therapeutic penetrating keratoplasty.

The onset of symptoms in sympathetic ophthalmia usually occurs between 3 weeks and 6 months following surgery. In the present patient, the symptoms in the sympathising eye occurred 2 months after surgery. The vision in the inciting eye was restricted to perception of light with defective projection of rays. Determination of any reduction of vision in the inciting eye was not possible, although there was an increase in inflammation in that eye. Enucleation of the inciting eye was deferred, as the patient withheld consent. Enucleation is reported to be useful only if performed early, within 2 weeks of the onset of symptoms.[8]

The symptoms described here resemble those of Vogt-Koyanagi-Harada (VKH) syndrome or posterior scleritis because of the presence of exudative retinal detachment. However, patients with VKH have no history of trauma, which is the only differentiating feature clinically. VKH and sympathetic ophthalmia, described as part of 'a spectrum of uveitis',[9] are both T-cell mediated diseases but sympathetic ophthalmia is incited by penetrating trauma whereas VKH has a spontaneous onset. Posterior scleritis is often related to rheumatoid arthritis and the patient may present with pain and exudative retinal detachment. There may even be subretinal exudates resembling the Dalen-Fuchs nodules of sympathetic ophthalmia, similar to those observed in the present patient. In such patients, ultrasonography demonstrates thickening of the sclera and choroid, which was absent here. Uveal effusion

syndrome was another possible diagnosis. However, the latter condition is characterised by peripheral choroidal separation and secondary retinal detachment and the choroid was clearly attached in the present case.

The cause of sympathetic ophthalmia in the patient reported here cannot be ascertained definitively. Although it appears likely that the inciting event was therapeutic penetrating keratoplasty and subsequent inflammation, uveal tissue prolapse may also have been an inciting factor. This case stresses the need for surgeons to fully explain the risks involved to patients undergoing therapeutic penetrating keratoplasty and to be alert to the possibility of sympathetic ophthalmia in the event that the patient develops visual complaints in the better eye.

References

1. Liddy L, Stuart J. Sympathetic ophthalmia in Canada. Can J Ophthalmol. 1972;7:157-9.
2. Bechrakis NE, Muller-Stolzenburg NW, Helbig H, Foerster MH. Sympathetic ophthalmia following laser cyclocoagulation. Arch Ophthalmol. 1994;112:80-4.
3. Margo CE, Pautler SE. Granulomatous uveitis after treatment of a choroidal melanoma with proton-beam irradiation. Retina. 1990; 10:140-3.
4. Pollack AL, McDonald HR, Ai E, et al. Sympathetic ophthalmia associated with pars plana vitrectomy without antecedent penetrating trauma. Retina. 2001;21:146-54.
5. Gass JD. Sympathetic ophthalmia following vitrectomy. Am J Ophthalmol. 1982;93:552-8.
6. Lubin JR, Albert DM, Weinstein M. Sixty-five years of sympathetic ophthalmia. A clinicopathologic review of 105 cases (1913–1978). Ophthalmology. 1980:87;109-21.
7. Dada T, Kumar A, Sharma N. Sympathetic ophthalmia associated with antecedent adherent leucoma – a rare association. Acta Ophthalmol Scand. 1998;76:380-1.
8. Reynard M, Riffenburgh RS, Maes EF. Effect of corticosteroid treatment and enucleation on the visual prognosis of sympathetic ophthalmia. Am J Ophthalmol. 1983:96;290-4.
9. Chan CC. Relationship between sympathetic ophthalmia, phacoanaphylactic endophthalmitis, and Vogt-Koyanagi-Harada disease. Ophthalmology. 1988:95:619-24.

Concurrent Congenital Rubella Cataract and Glaucoma

Arvind Gupta, Subashini Kaliaperumal, Renuka Srinivasan, Datta Gulnar Pandian
Department of Ophthalmology, Jawaharlal Institute of Postgraduate Medical Education and Research, Pondicherry, India

This report is of a patient with congenital rubella syndrome with microphthalmos and cataract in 1 eye and raised intraocular pressure with an apparently normal-sized cornea in the fellow eye. Enzyme-linked immunosorbent assay for detection of rubella immunoglobulin M and immunoglobulin G antibodies was positive. The cataracts were removed by manual irrigation and aspiration with primary posterior capsulotomy and limited anterior vitrectomy. The raised intraocular pressure was managed by trabeculotomy and trabeculectomy.

Key words: *Cataract, Hydrophthalmos, Microphthalmos, Rubella syndrome, congenital*

Asian J Ophthalmol. 2007;9:92-3

Introduction

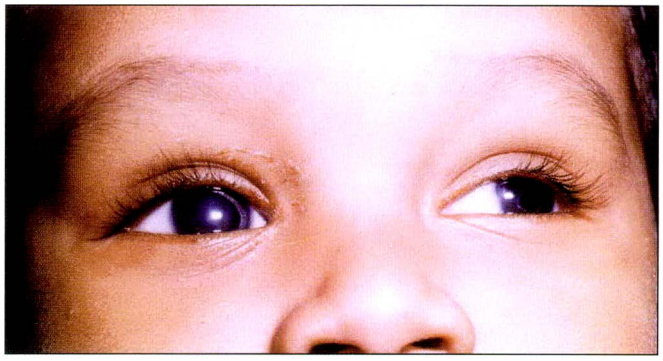
Rubella infection in a pregnant woman can affect the development and functioning of the foetal eye as well as other body organs. Various manifestations of congenital rubella infection are collectively classified as congenital rubella syndrome (CRS). Ocular manifestations of CRS include congenital cataract, chorioretinopathy, microphthalmos, strabismus, and corneal clouding.[1] Cataract, the most frequent presenting feature of CRS, is usually bilateral. Congenital glaucoma, an infrequent finding of CRS, poses a diagnostic challenge as the associated microphthalmos may mask corneal enlargement.[2]

Cataract is considered to be a manifestation of early rubella infection in pregnancy, while glaucoma is a manifestation of late infection. This report is of 1 of 2 patients treated at the Department of Ophthalmology, Jawaharlal Institute of Postgraduate Medical Education and Research, Pondicherry, India, for CRS with unilateral microphthalmos (Figure 1) and cataract in 1 eye and clear lens with glaucoma in the fellow eye.

Case Report

A 3-day-old neonate was referred to the Department of Ophthalmology in 2004 after white reflex was noted in the right eye by the neonatologist. The mother gave a history of rash with a sore throat lasting for 3 days during the first month of pregnancy. At 36 weeks, she was diagnosed with oligohydramnios and the foetus was delivered by caesarean section. The neonate had intrauterine growth retardation, with a birth weight of 1.45 kg, and was treated in the Neonatal Intensive Care Unit for 5 days. Evaluation under general anaesthesia revealed a microcornea measuring 8 x 9.5 mm in the right eye. There was dense nuclear cataract involving the visual axis precluding fundus evaluation. The left cornea was clear and measured 12.0 x 11.5 mm. The lens was clear and fundus examination showed a cup-disc ratio of 0.6. There was no associated pigmentary retinopathy. Gonioscopy of the right eye with the Koeppe lens showed anterior insertion of the iris with angles of 2 in the superior and nasal quadrants and 3 in the other 2 quadrants (Shaffer's grading); the left eye also showed anterior insertion of the iris into the trabeculum, with prominent iris processes in all 4 quadrants. The intraocular pressures (IOPs) were 11 mm Hg and 32 mm Hg in the right and left eyes, respectively. Systemic evaluation revealed the presence of patent ductus arteriosus. Serology showed elevated immunoglobulin M (Ig M) and Ig G antibodies against rubella.

Figure 1. Microphthalmos in the right eye of a 9-month-old infant with congenital rubella syndrome.



Correspondence: Dr Arvind Gupta, Department of Ophthalmology, Jawaharlal Institute of Postgraduate Medical Education and Research, Pondicherry-605 006, India.
Tel: (91 413) 200 2371; Fax: (91 413) 227 2067;
E-mail: arvind_ophthal@yahoo.co.in

Trabeculotomy and trabeculectomy were performed in the left eye for glaucoma and the cataract in the right eye was managed by manual irrigation and aspiration with primary posterior capsulotomy and limited anterior vitrectomy. Evaluation under general anaesthesia performed at 3 months follow-up showed IOPs of 13 mm Hg in both eyes and, after 1 year, the IOPs were 13 mm Hg and 14 mm Hg in the right and left eyes, respectively. The right eye was prescribed a contact lens for aphakia.

Discussion

Rubella infection during pregnancy causes multisystem dysfunction, including deaf-mutism, cataract, growth retardation, microcephaly, congenital glaucoma, chorioretinopathy, cardiac defects, and delayed developmental milestones.[1] The risk for foetal infection varies with the time of maternal infection. Foetal infection occurs in 81% of infants exposed in the first trimester, 30% to 40% of those exposed in the second trimester, and 40% to 100% of infants exposed in the third trimester.[3] This variation may be due to the changes in placental structure, leading to increased resistance in the second trimester, while free passage of maternal and foetal blood towards term may increase the risk of transmission.[4]

Cataract formation in CRS is due to the virus entering the lens before the development of the lens capsule that would otherwise act as a barrier to the virus. The virus enters the lens before the closure of the foetal fissure, although there is a low risk for lenticular infection following foetal viraemia due to the presence of hyaloid vessels.[5] The virus in the lens tissue continues to replicate and high concentrations are found in cataractous lenses. The virus can persist in these cataractous lenses for up to 3 years postnatally.[6]

Glaucoma in CRS results from failure of absorption of the mesoderm of the angle or failure of Schlemm's canal to differentiate. Thus, glaucoma is due to maternal infection contracted during late pregnancy. The retina and other ocular structures are not protected by a capsule and remain vulnerable during the entire pregnancy.

Rarely, the virus may enter the embryonic cells and is thus transferred to their progeny during cell proliferation, resulting in infected clones of cells.[7] The immunological response of the foetus to rubella may be handicapped by infection of the primitive immune cells.[8] These infected cells may interfere with the normal proliferation of different ocular tissues leading to microphthalmos.

Persistence of the virus in foetal cells due to an impaired foetal immune response may explain the concurrent occurrence of cataract in 1 eye and glaucoma in the other. Buphthalmos may not manifest in CRS due to associated microphthalmos. Thus, patients with unilateral microphthalmos should be examined for glaucoma in the fellow eye. Correct immunisation and increased awareness of the effects of rubella infection can prevent infants being born with CRS.

References

1. Vijayalakshmi P, Kakkar G, Samprathi A, Banushree R. Ocular manifestations of congenital rubella syndrome in a developing country. Indian J Ophthalmol. 2002;50:307-11.
2. Swan C. Congenital malformations in infants following maternal rubella in pregnancy. Trans Ophthal Soc Aust. 1944;4:182-49.
3. Miller E, Cradock-Watson JE, Pollock TM. Consequences of confirmed maternal rubella at successive stages of pregnancy. Lancet. 1982;ii: 781-4.
4. Kaplan C. The placenta and viral infections. Semin Diag Pathol. 1993; 10:232-50.
5. Karkinen-Jaaskelainen M, Saxen L, Vaheri A, et al. Rubella cataract in vitro: sensitive period of the developing human lens. J Exp Med. 1975; 141:1238-48.
6. Menser MA, Harley JD, Hertzberg R, et al. Persistence of virus in lens for three years after prenatal rubella. Lancet. 1967;2:387-8.
7. Rawls WE, Desmyter J, Melnick JL. Virus carrier cells and virus free cells in fetal rubella. P Soc Exp Biol Med. 1968;129:477-83.
8. South MA, Sever JL. Teratogen update: the congenital rubella syndrome. Teratology. 1985;31:297-307.

Siderosis Bulbi after Forgotten Intraocular Injury with an Iron-containing Foreign Body

Sunil Kumar
Mohammad Dossary Hospital, Al Khobar, Saudi Arabia

Siderosis bulbi is a rare condition that is often a sequel to a retained iron-containing intraocular foreign body. This report describes a 28-year-old man in whom siderosis bulbi developed 6 months after a forgotten intraocular injury with a foreign body.

Key words: *Foreign bodies, Siderosis*

Asian J Ophthalmol. 2007;9:94-6

Introduction

Siderosis bulbi is a rare condition occurring as a result of a retained iron-containing intraocular foreign body. Most patients with intraocular foreign body are treated before they develop siderosis. However, a trivial injury caused by an iron-containing intraocular foreign body that goes untreated may result in siderosis bulbi. Low-grade inflammation, a solitary sign of siderosis-like heterochromia, or a dilated pupil due to the retained foreign body may cause a diagnostic dilemma. Accurate diagnosis and timely removal of the foreign body may avert the grave visual prognosis associated with advanced siderosis bulbi.

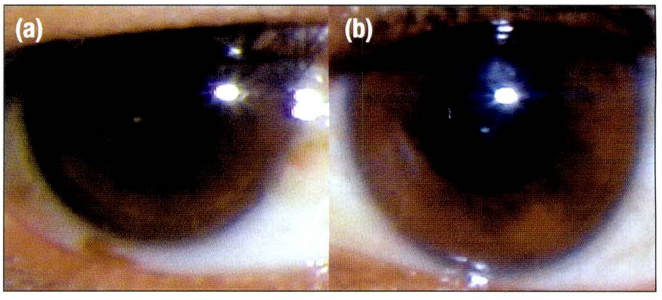
Case Report

A 28-year-old man from Bangladesh was referred to the Mohammad Dossary Hospital, Al Khobar, Saudi Arabia, in 2006 with progressive painless decrease of vision in the right eye for 10 weeks. He was being treated at a polyclinic for a provisional diagnosis of chronic iridocyclitis. He had no history of diabetes or hypertension. At examination, his best corrected visual acuity was 6/12 and 6/6 in the right and left eyes, respectively. The intraocular pressure of each eye was within normal limits. The pupils of both eyes were reacting to light, and no relative afferent pupillary defect was seen. The right eye exhibited conjunctival congestion, non-granulomatous keratic precipitates on an otherwise clear cornea, a moderate reaction of 2+ cells in the anterior chamber and vitreous, and mild macular oedema.

In the absence of a strong suspicion of a systemic disease manifesting as uveitis, this patient was not investigated further.

Correspondence: Dr Sunil Kumar, Mohammad Dossary Hospital, Al Khobar 31952, Eastern Province, Saudi Arabia.
Tel: (96 63) 894 5524; Fax: (96 63) 895 0735;
E-mail: sunkaru79@hotmail.com

Figure 1. Heterochromia iridis due to hyperchromia of the right iris as a sequel to retained metallic intraocular foreign body.



Treatment was commenced with prednisolone 1% eye drops every hour and prednisolone 0.5% ointment at night.

After 5 days of treatment, the anterior chamber reaction remained unchanged. As the iridocyclitis was not resolving with topical medication, oral prednisolone was added at a dose of 40 mg/day and tapered by 10 mg every third day. A fasting blood glucose test and chest X-ray were within normal limits.

After 1 week, the anterior chamber reaction resolved, but there was no improvement in visual acuity. A subtle change in the colour of the right iris was noted (Figure 1). A provisional diagnosis of Fuchs' uveitis syndrome was made, and the treatment plan was continued. The patient was re-examined 12 days later, when a ring of brown spots was noticed around a large brown spot in the centre, under the anterior lens capsule, along with early cataract in the right eye (Figures 2 and 3). At this point, the patient admitted that his right eye had been injured by an unknown object approximately 6 months prior to the onset of the condition. At the time, he had obtained over-the-counter medication and his eye appeared to heal after a few days.

X-ray of the skull showed a radio-opaque intraocular foreign body (Figures 4 and 5). Dilated indirect ophthalmoscopic examination revealed pigmentary changes of the inferior peripheral retina.

Figure 2. Ring of brown-coloured spots midway between the anterior pole and equator of lens.

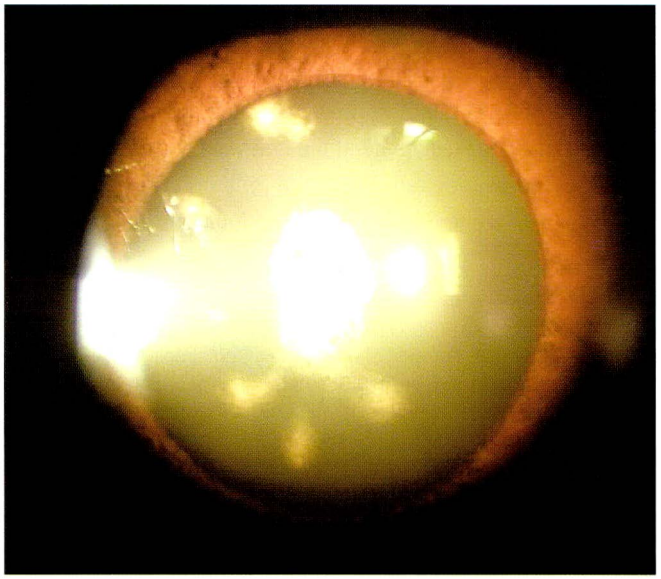
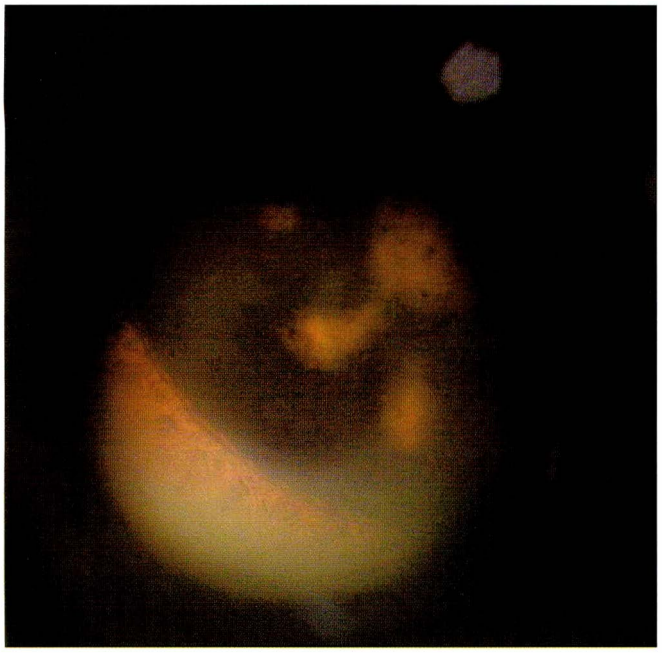


Figure 3. Brown-coloured spot under the anterior lens capsule.



The patient was diagnosed with siderosis bulbi. Despite meticulous examination, it was not possible to locate the point of entry of the foreign body.

Discussion

Siderosis bulbi is a rare sight-threatening complication of retained iron-containing foreign body.[1] The time interval between the entrance of a foreign body and the first appearance of outward signs of siderosis bulbi varies from 18 days to 8 years after an intraocular injury.[2]

Figure 4. X-ray of the orbit (para-nasal sinus view) depicting a metallic intraocular foreign body.

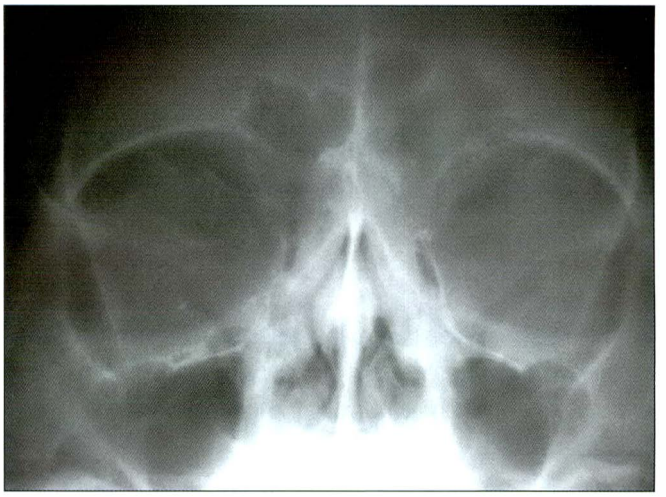
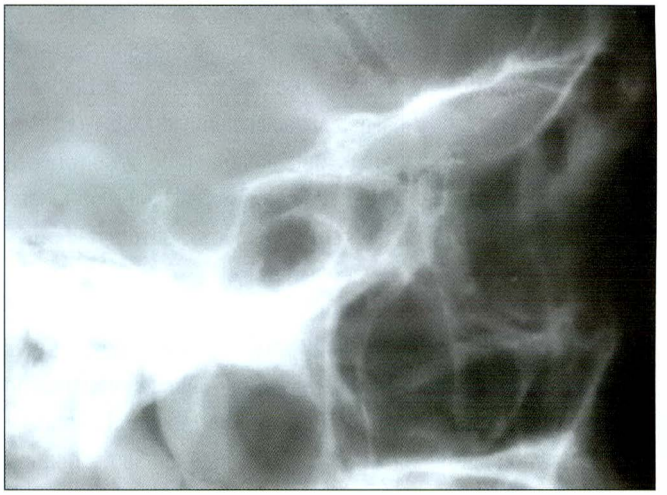


Figure 5. Lateral X-ray of the orbit showing a tiny metallic intraocular foreign body.



Although the nature of intraocular foreign bodies varies, the majority are magnetic and metallic. The most common cause of intraocular foreign body is a hand-wielded hammer and chisel.[3]

The presence of an intraocular foreign body after eye trauma may not be readily apparent. Patients often present only after the onset of visual disturbances. Serious complications of intraocular foreign body include endophthalmitis, cataract, retinal detachment, and siderosis bulbi.[4]

Siderosis bulbi is characterised clinically by brown pigmentation of the iris, lens capsule and vitreous, and by pupillary mydriasis, cataract, and retinal pigmentary degeneration.[5] In a patient with unexplained unilateral pupillary dilatation, the possibility of siderosis bulbi should be considered.[6]

Yellow-brown discoloration of the iris may present as heterochromia iridis. Heterochromia iridis and uveitis due to siderosis bulbi can be misdiagnosed as Fuchs' uveitis syndrome. The

presence of a non reactive pupil with heterochromia may help in distinguishing Fuchs' uveitis syndrome from siderosis bulbi — in siderosis bulbi, the involved eye shows hyperchromia, in contrast to hypochromia in Fuchs' uveitis syndrome. Unexplained heterochromia due to a retained intraocular foreign body may require computed tomography scan to delineate the presence and location of a foreign body missed by standard radiographic techniques.[7]

Iris discoloration is usually seen if yellow-brown dots occur under the anterior lens capsule.[8] These spots are round and usually less than 0.5 mm in diameter, and appear at regular intervals in a circle, in or under the anterior lens capsule at the anterior pole. Most patients with iron-containing intraocular foreign body develop siderotic cataract.[9]

The retina shows pigmentary degeneration in siderosis bulbi. Patients may develop a concentric constriction of the visual field[2,3] and colour vision defects.[8] If the foreign body is not removed, the visual prognosis is poor.

The encapsulation of an iron foreign body located in the retina and choroid, with focally circumscribed ocular siderosis bulbi and glial overgrowth of the retinal defect can be confused with malignant melanoma.[10] An intraocular non-metallic foreign body, surrounded by a fibrous capsule, can mimic the characteristics of a peripheral toxocara granuloma. The differential diagnosis of retained intraocular foreign body should be considered.[11]

Ocular inflammation after intraocular foreign body may develop some time after the injury and may vary from low-grade, chronic uveitis to severe endophthamitis. Delayed or unusual presentation of retained intraocular foreign body is a diagnostic challenge.[12] Gonioscopy and ultrasound biomicroscopy can be used to confirm the presence of anterior segment foreign bodies.[4] Specific changes in electroretinogram have been reported in siderosis bulbi. In particular, the electroretinogram exhibits reduced α and β waves for photopic and scotopic responses.

There are several reasons for the development of siderosis bulbi after intraocular injury with a foreign body — some patients do not attend for treatment as they have no discomfort; medical treatment may be inadequate at the first visit; and a small foreign body may be overlooked. Therefore, patients presenting with siderosis bulbi are to be expected in the future.

References

1. Vo Tan P, Korobelnik JF, D'Hermies F, Hoang-Xuan T. Ocular siderosis: its management. Apropos of a case. J Fr Ophtalmol. 1995;18:621-4.
2. Ghoraba H, al-Nahrawy O, Mohamed OA, et al. The non recordable electroretinogram in siderosis bulbi might not indicate poor visual outcome. Retina. 2001;21:277-9.
3. Schocket SS, Lakhanpal V, Varma SD. Siderosis from a retained intraocular stone. Retina. 1981;1:201-7.
4. Griffiths ML, Lee GA. Retained intraocular foreign body. Clin Exp Optom. 2004;87:34-6.
5. O'Dufty D, Salmon JF. Siderosis bulbi resulting from an intraocular foreign body. Am J Ophthalmol. 1999;127:218-9.
6. Scotcher SM, Canning CR, Dorrell D. Siderosis bulbi: an unusual cause of a unilaterally dilated pupil. Br J Hosp Med. 1995;54:110-1.
7. Barr CC, Vine AK, Martonyi CL. Unexplained heterochromia, intraocular foreign body demonstrated by computed tomography. Surv Ophthalmol. 1984;28:409-11.
8. Welch RB. Two remarkable events in the field of intraocular foreign body: (1) The reversal of siderosis bulbi. (2) The spontaneous extrusion of an intraocular copper foreign body. Trans Am Ophthalmol Soc. 1975;73:187-203.
9. Sneed SR, Weingeist TA. Management of siderosis bulbi due to a retained iron-containing intraocular foreign body. Ophthalmology. 1990;97:375-9.
10. Lang GK, Volcker HE, Naumann GO. Strictly focal siderosis bulbi posterior. Klin Monatsbl Augenheilkd. 1987;191:137-9.
11. Papa-Oliva G, Leizaola C, Rivera J, et al. Retained intraocular foreign body. an unusual presentation. Arch Soc Esp Oftalmol. 2005;80:425-8.
12. McGimpsey SJ, Rankin SJ. Presentation of intraocular foreign body 25 years after the event. Clin Experiment Ophthalmol. 2005;33:665-6.

20th APACRS Annual Meeting

Hanoi, Vietnam, 28-30 September 2007

The Asia Pacific region has emerged as one of the most important economic centres in recent years and Vietnam is notably one of the fastest growing economies in Asia. Vietnam's progress in the economic sphere is reflected in improved skills and technological advances in ophthalmology. We are delighted this year to be holding the 20th Asia Pacific Association of Cataract and Refractive Surgeons (APACRS) Annual Meeting in conjunction with the 50th Anniversary meeting of the National Institute of Ophthalmology in Hanoi and the Vietnamese Ophthalmological Society.

This meeting will be the largest international conference to be held in Vietnam and delegates will benefit from the superb educational programme and teaching courses provided. One of the highlights of the programme is the unique joint plenary which brings the confluence of world renowned speakers from 3 major cataract and refractive societies; namely the APACRS, the American Society of Cataract and Refractive Surgeons (ASCRS), and the European Society of Cataract and Refractive Surgeons (ESCRS).

The annual APACRS meeting provides a unique environment for regional and international ophthalmologists to share knowledge and friendship. Delegates attending the meeting will not only benefit from the educational activities but will also have the opportunity to experience the unique cultural and historical heritage of Hanoi.

For further information, contact the secretariat at: **apacrs2007@snec.com.sg** or visit the website at: **www.apacrs2007.org**

45th Annual Symposium of the ISCEV

Hyderabad, India, 25-29 August 2007

The new millennium is witness to amazing developments in technology that have expanded our horizons in ophthalmology. Keeping updated is a prerequisite to providing cutting-edge care to patients. We at the Retina Services of LVPEI are greatly honoured that the International Society for Clinical Electrophysiology of Vision (ISCEV) has given us the opportunity to host its 45th Annual Symposium in Hyderabad, India, in August 2007.

This symposium has a 45-year history and a tradition of being a forum to learn, share, and bring together masters and students in the field of clinical electrophysiology of vision in a congenial and informal educational environment. This is a golden opportunity for colleagues to participate, especially those who have fewer opportunities to attend international conferences of this calibre.

The focus this year is on use of electrophysiology to define genotype-phenotype correlations and the evolving role of various types of VEP recordings. However, the varied programme, spread over 5 days, goes beyond the focused themes and includes didactic lectures by eminent faculty, free papers, dedicated poster sessions, special lectures on animal electrophysiology, clinical drug development and ocular toxicity evaluations, and clinical case sessions. The icing on the cake is a 2-day preconference hands-on course run by distinguished members of the society. A bonus is the trade exhibition involving all the major electrodiagnostic equipment manufacturers. It is expected that the conference deliberations will be a wonderful opportunity for a wide audience who have had limited exposure to these engaging techniques; techniques that are often the tools to unlock the many baffling signs and symptoms seen in clinical practice.

Objectives

- To promote clinical use of various techniques of visual electrophysiology.
- To promote interaction among scientists and clinicians towards better understanding of electrophysiology techniques in human and animal visual physiology and pathological states.

Important Information

Early bird registration ends:	3 June 2007
Registration at conference site:	Subject to availability
ISCEV course registration:	60 candidates
Abstract submission deadline:	15 April 2007
Abstract acceptance information:	6 May 2007
Travel grant application deadline:	1 April 2007

For further information, contact the secretariat at: **Subhadra@Lvpei.Org** or visit the website at: **www.Iscev2007.Org?Ophthalmology**

June 2007

9-12
2007 Congress of the European Society of Ophthalmology
Vienna, Austria
Contact: Britta Sjöblom
Tel: (46 84) 596 650
Fax: (46 86) 619 125
E-mail: britta.sjoblom@congrex.se

16-18
Indonesian Ophthalmologist Association Annual Meeting
Jakarta, Indonesia
Contact: Johnny Zulkarnain
Tel: (62 21) 315 8926
Fax: (62 21) 391 9594
E-mail: pit33jakarta@perdami.or.id

20
Asia Pacific Society of Ophthalmic Plastic and Reconstructive Surgery Annual Meeting
Seoul, Korea
Contact: Dr Sang In Khwarg
E-mail: khwarg2000@yahoo.com

21-22
Korean Society of Ophthalmic Plastic and Reconstructive Surgery International Symposium
Seoul, Korea
Contact: Dr Sang In Khwarg
E-mail: khwarg2000@yahoo.com.

30-2 July
7th ISOHK International Symposium of Ophthalmology
Hong Kong
Contact: Ms Carol Yeung
Tel: (852) 2762 3185
Fax: (852) 2194 0695
E-mail: carolyeung@cuhk.edu.hk

July 2007

18-21
World Glaucoma Congress
Singapore
Contact: Congress Organizer/Scientific Secretariat
Tel: (31 20) 679 3411
Fax: (31 20) 673 7306
E-mail: meetingoffice@globalaigs.org
Website: www.globalaigs.org

August 2007

25-29
2007 Annual Symposium of the International Society for Clinical Electrophysiology of Vision (ISCEV)
Hyderabad, India
Contact: Dr Subhadra Jalali, Secretariat
Tel: (091 040) 3061 2607
Fax: (91 040) 2354 8271
E-mail: Subhadra@Lvpei.Org
Website: www.Iscev2007.Org?Ophthalmology

September 2007

8-12
XXV Congress of the ESCRS
Stockholm, Sweden
Contact: Congress Secretariat
Tel: (353) 1209 1100
Fax: (353) 1209 1112
E-mail: escrs@escrs.org
Website: www.escrs.org

28-30
Asia Pacific Association of Cataract and Refractive Surgeons Annual Meeting
Hanoi, Vietnam
Contact: Secretariat
E-mail: apacrs2007@snec.com.sg
Website: www.apacrs2007.org

November 2007

10-13
2007 Annual Meeting of the American Academy of Ophthalmology (AAO)
New Orleans, USA
Contact: American Academy of Ophthalmology
Tel: (1 415) 561 8500
Fax: (1 415) 561 8533
E-mail: aaoe@aao.org
Website: www.aao.org/annual_meeting/2006.cfm

24-28
2007 National Congress Of The Royal Australian & New Zealand College Of Ophthalmologists
Perth, Australia
Contact: Congress West
Tel: (61 89) 389 6906
Fax: (61 89) 389 1234
E-mail: Conwes@Congresswest.Com.Au
Website: www.Congresswest.Com.Au/Ranzco2007?Ophthalmology

Note to Readers
This section is intended to highlight activities of interest to glaucoma specialists and ophthalmologists in Asia. Please let us know of any forthcoming activities that you may be organising or wish to feature on this section.

December 2007

2-4
Asian Oceanic Glaucoma Society 2007
Bangkok, Thailand
Contact: Secretariat
E-mail: tenkn@mahidol.ac.th

7-8
Retinal and Glaucoma Imaging 2008: Ocular Coherence Tomography (OCT) Applications and Future Technology
Palm Beach, FL, USA
Contact: Department of CME, Bascom Palmer Eye Institute Dept. of CME
Tel: (1 305) 326 6110
Fax: (1 305) 326 6518
E-mail: bpeicme@med.miami.edu
Website: www.bascompalmer.org

May 2008

21-24 May
18th International Visual Field & Imaging Symposium (IPS2008)
Nara, Japan
Contact: Chota Matsumoto
Tel: (81 72) 366 0221
Fax: (81 72) 368 2559
E-mail: ips2008@med.kindai.ac.jp

June 2008

28-2 July
World Ophthalmology Congress
Hong Kong
Contact: Ms Angela Cho
Tel: (852) 2762 3128
Fax: (852) 2194 0695
E-mail: angelacho@woc2008hongkong.org
Website: www.woc2008hongkong.org/

Asian Journal of OPHTHALMOLOGY is the official publication of the South East Asia Glaucoma Interest Group. The Journal is a peer-reviewed publication and is published bimonthly in February, April, June, August, October, and December. All articles that contribute to the development and understanding of ophthalmology in Asia will be considered. The Journal is indexed in EMBASE/Excerpta Medica.The Journal welcomes contributions within the categories of original research, invited papers, review articles, case reports, conference reports, and letters to the editor. Submissions may be made online at www.seagig.org or sent by e-mail to manuscripts@seagig.org or may be sent on disk to the following address:

The Editor
Asian Journal of OPHTHALMOLOGY
Scientific Communications International Ltd
Suite C, 10/F, Wo On Building
10 Wo On Lane, Central, Hong Kong
E-mail: editor@seagig.org

Manuscript Criteria

Submitted manuscripts should adhere to the stated format. Manuscripts that do not conform to the approved format will be returned without review. Authors should fulfil the authorship criteria stated in the *Uniform requirements for manuscripts submitted to biomedical journals: writing and editing for biomedical publication,* which should also be followed for general guidance.[1] A covering letter stating that the submitted material has not been previously published and is not under consideration for publication elsewhere should be included. The receipt of submissions will be acknowledged. All accepted papers become the permanent property of *Asian Journal of OPHTHALMOLOGY* and may not be published elsewhere without written permission from the Journal.

Categories of Articles

Editorials — Length should not exceed 1000 words; the total number of Tables and Figures should not be more than 2, and references not more than 10.

Original Articles — Length should not exceed 2500 words; the total number of Tables and Figures should not be more than 6, and references not more than 40. Headings of Introduction, Patients and Methods, Results, and Discussion should be included.

Review Articles — Length should not exceed 2500 words; the total number of Tables and Figures should not be more than 6, and references not more than 40. Section headings should be provided.

Case Reports — Length should not exceed 1000 words; the total number of Tables and Figures should not be more than 2, and references not more than 10.

Conference Reports — Length should not exceed 2500 words; the total number of Tables or Figures should not be more than 6, and references not more than 40. Headings for different sections should be provided.

Letters to the Editor — Communications on all aspects of ophthalmology are encouraged. Length should not exceed more than 300 words, and references should number no more than 5.

Manuscript Preparation

The manuscript should be arranged as follows:

Title Page

The title page should contain the following:

- the title of the article, which should be concise but informative
- a short running title of fewer than 40 characters (including spaces)
- the first name, middle initials, and last name of all authors, with their 2 highest academic degrees; a maximum of 6 authors is permitted
- the name of the department(s) and institution(s) to which each author is affiliated
- the full name, address, telephone and fax numbers, and e-mail address of the designated author for correspondence.

Abstract and Key Words

The abstract for original articles must summarise the purpose, procedures, main findings, and principal conclusions of the investigation, and must be structured with the following subheadings: Aim(s), Patients and Methods, Results, and Conclusion(s). Abstracts for all other articles must be unstructured, but should include the key points discussed in the paper. Abstracts should be no longer than 250 words. The key words must be Medical Subject Headings taken from Medline/*Index Medicus*.

Body Text

For original articles, the following sections should be included:

Introduction

The rationale for the study should be summarised and pertinent background material outlined. This should not include findings or conclusions.

Patients and Methods

This section should describe the methodology in sufficient detail to leave the reader in no doubt as to how the results are derived.

Manuscripts that contain the results of human or animal studies should make clear that a high standard of ethics was applied. Invasive studies of humans should state that the research protocol was approved by the local ethics committee.

Results

The results should be presented in logical sequence in the text, Tables, and Figures; repetitive presentation of the same data in different forms should be avoided. This section should not include material appropriate to the Discussion. Results must be statistically analysed where appropriate, and the statistical guidelines of the International Committee of Medical Journal Editors should be followed.[1]

Discussion

Data given in the Results section should not be repeated here. This section should present the implications and limitations of the study. The Discussion may also include

an evaluation of methodology and of the relationship of new information to the existing body of knowledge in the field. Conclusions should be incorporated into the final paragraph and should be consistent with — and completely supported by — data in the text.

Acknowledgement(s)

Acknowledgements can be made to people who have offered assistance in the research or preparation of the manuscript and who do not fulfil authorship criteria. Research or project support should also be stated, as well as any conflicts of interest.

References

The references should be numbered in numerical order in the text and the reference list, and should not appear in alphabetical order. References should follow the *Uniform requirements for manuscripts submitted to biomedical journals: writing and editing for biomedical publication*[1] and should appear in the text, Tables, and Figures as Arabic numerals in superscript. Journal titles should be abbreviated in accordance with Medline/ *Index Medicus*. Authors are responsible for the accuracy of references and must verify them against the original documents. All authors and editors must be listed. The following are examples of reference style:

Standard journal article

Cheung JC, Wright MM, Murali S, Pederson JE. Intermediate-term outcome of variable dose mitomycin C filtering surgery. Ophthalmology 1997;104:143-149.

Supplement

Taylor A, Jacques PF, Epstein EM. Relations among aging, antioxidant status, and cataract. Am J Clin Nutr 1995;62 (6 Suppl): 1439-1447.

Books and other monographs

Kupfer C, Underwood B, Gillen T. Leading causes of visual impairment worldwide. In: Albert DM, Jakobiec FA, editors. Principles and practice of ophthalmology. Philadelphia: WB Saunders Company; 1994: 1250-1251.

Tables

Tables must be typed in Table format after the references or provided in a separate Microsoft Word file. All Tables must be cited in numerical order in the text. A brief title should be supplied for each Table and a short heading provided for each column. Explanatory matter should be placed in footnotes, not in the heading. Abbreviations should be avoided in Tables. If abbreviations are necessary, they must be explained in a footnote. Statistical measures of variation such as standard deviation, standard error of the mean, and confidence interval should be identified in the column headings.

Figures and Illustrations

All Figures must be cited in numerical order in the text, and a brief legend provided after the references. Figures should be provided in electronic format in a separate file, not as part of the body text. The resolution of Figures must be at least 350 dpi. When symbols, arrows, numbers, or letters are used to identify part of an illustration, each one should be identified and clearly explained in the legend. If only hard copies of Figures are submitted, each one should have a label pasted on the back indicating the number of the Figure, the author's name and the top of the Figure (Figures must not be written on and paper clips must not be used).

Illustrations can include photographs, photomicrographs, charts, and diagrams. Photographs of persons must be retouched to make the subject unidentifiable, and be accompanied by written permission from the subject to use the photograph. Footnotes for Figures and Tables must use the following symbols, in this order: *, †, ‡, §, ‖, ¶, **, ††, ‡‡, §§, ‖‖, ¶¶.

The corresponding author is responsible for obtaining written permission to use any copyrighted text or illustrations.

General Style

The following style should be used:

- all papers should be written in English; spelling should comply with the Concise Oxford English Dictionary
- Arabic numerals should be used for all numbers, except for numbers below 100 at the beginning of sentences, which should be spelled out
- abbreviations should not appear in the title or abstract and their use in the text should be limited; abbreviations should be defined at the first mention in the text unless they are standard units of measurement
- Système International (SI) measurements must be used for all laboratory values
- generic drug names must be used unless the specific trade name of a study drug is directly relevant to the discussion.

Editorial Processing

All manuscripts submitted to *Asian Journal of OPHTHALMOLOGY* will be assessed by peer review to determine their suitability for publication. Some manuscripts may require revision before acceptance for publication; in this case, reviewers' comments will be forwarded to the author. The Editor makes the final decision regarding acceptance of a manuscript for publication. Papers should be submitted exclusively to *Asian Journal of OPHTHALMOLOGY*. If accepted for publication, copyright for the manuscript and all parts will be assigned to *Asian Journal of OPHTHALMOLOGY*.

Accepted manuscripts will be copy edited according to the Journal style and returned to the author for approval prior to publication. Authors are responsible for all statements made in their work, including changes made by the copy editor.

Reference

1. International Committee of Medical Journal Editors (ICMJE). Uniform requirements for manuscripts submitted to biomedical journals: writing and editing for biomedical publication. ICMJE; 2004. Available from: http://www.icmje.org

Association of International Glaucoma Societies

THE GLOBAL GLAUCOMA NETWORK

AIGS
WORLD GLAUCOMA CONGRESS

www.GlobalAIGS.org

Singapore, July 18-21 2007

FOR POWERFUL INCREMENTAL IOP REDUCTION AFTER INITIAL MONOTHERAPY

1-drop-daily XALACOM provides your patients with

- ***Powerful incremental intraocular pressure (IOP) reduction***[1,2]
- ***Tolerability that supports therapeutic goals***
- ***Added power without the added drops***

XALACOM is indicated for the reduction of IOP in patients with open-angle glaucoma and ocular hypertension who are insufficiently responsive to topical beta-blockers.

XALACOM is contraindicated in patients with reactive airway disease, including bronchial asthma, a history of bronchial asthma, or severe chronic obstructive pulmonary disease; sinus bradycardia; second- or third-degree atrioventricular block; overt cardiac failure; cardiogenic shock; or hypersensitivity to any component of this product.

XALACOM has been reported to cause changes to pigmented tissues. The most frequently reported changes have been increased pigmentation and growth of eyelashes. The iris pigmentation changes may be permanent.

In the 6-month registration trials, the most frequent adverse events were eye irritation, including stinging, burning, and itching (12.0%); eye hyperaemia (7.4%); corneal disorders (3.0%); conjunctivitis (3.0%); blepharitis (2.5%); eye pain (2.3%); headache (2.3%); and skin rash (1.3%).

Please refer to product insert for full prescribing information.

References:
1. Higginbotham EJ, Feldman R, Stiles M, Dubiner H, for the Fixed Combination Investigative Group. Latanoprost and timolol combination therapy vs monotherapy: one-year randomized trial. *Arch Ophthalmol.* 2002;120:915-922. 2. Data on file. Pfizer Inc, New York, NY.

Once Daily Xalacom™
latanoprost/timolol maleate
1 Drop for Incremental Power

Pfizer

Suite 701, Pacific Place,
88 Queensway,
Hong Kong