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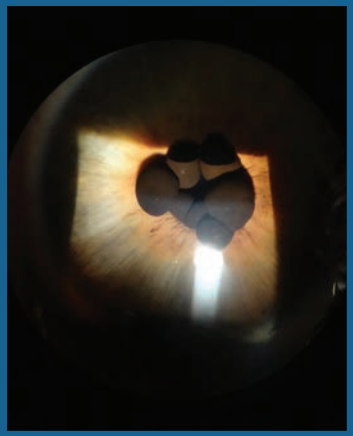

Iris pigment epithelial cysts.

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Laser puncture of symptomatic primary iris pigment epithelial cyst causing hemeralopia: a rare case

Ram Lal Sharma, Mohan Lal Pandey, Vinod Sharma, Kalpana Sharma, Neha Chowdhary
Indira Gandhi Medical College & Hospital, Shimla, Himachal Pradesh, India

Abstract
Primary iris pigment epithelium cysts involve posterior surface of the iris and can occur at pupillary margin or anterior ciliary body. They may be stationary or progressive and sometimes regress spontaneously. These cyst can occasionally lead to angle-closure glaucoma, plateau iris syndrome and secondary pigment dispersion syndrome. A steadily growing cyst may disturb the vision by covering the visual axis and provoke an increase in intraocular pressure (IOP) or even inflammation if it touches the corneal endothelium. There are multiple management options in complicated situations. We report a case of a 17-year-old girl with unusual complaints of hemeralopia and dark-brown discolouration of pupils in both eyes. On examination, she had multiple pigment epithelial iris cysts at the pupillary margins, which were punctured with Nd:Yag laser, and the response was improvement in vision and hemeralopia without any pigment dispersion or IOP changes.

Keywords: *Nd:Yag laser, primary iris pigment epithelium*

Introduction

Primary iris cyst involves a portion of iris, which is lined by pigment epithelium, while secondary iris cyst are results of some pathology like trauma, inflammations, metastasis, parasites or miotic therapy. Primary iris cysts are less common and mostly congenital, which could be stromal or pigment epithelial cysts. They are of neuroepithelial origin and involve the iris pigment epithelium (IPE) and the ciliary body. Central cysts are rare and account for approximately 3% of all primary IPE cysts.[1] We report a case of bilateral, central pigment epithelial cysts of the iris causing hemeralopia, and cosmetic concern to the patient.

Case

We report a case of a 17-year-old girl presented with complaints of difficulty in seeing in bright sunlight and brownish discolouration of pupils of both eyes. On slit lamp examination, there were seven visible dark-brown iris cysts with smooth

Correspondence: Dr. Ram Lal Sharma, Professor, Department of Ophthalmology, IGMC, Shimla, Himachal Pradesh, India.
E-mail: rls_10@rediffmail.com

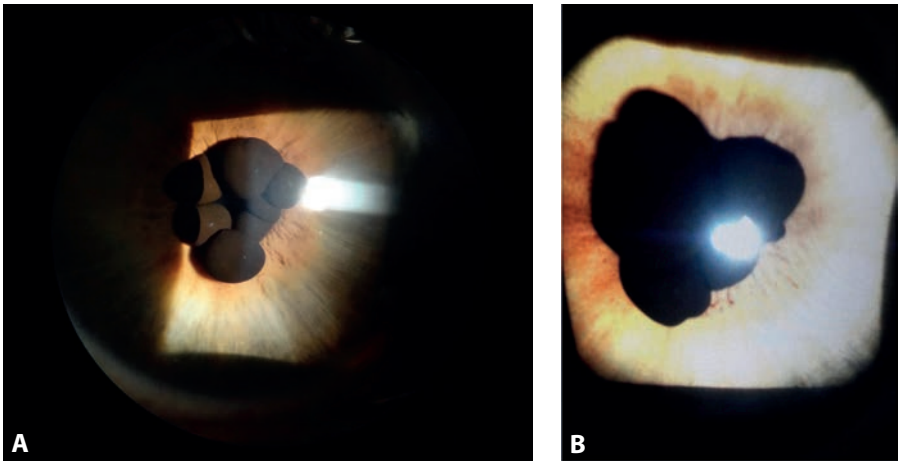

Fig. 1. (A and B): Iris pigment epithelial cysts of right and left eyes.

surface of varying size ranging from 1 to 3 mm in right eye and six cysts in left eye. They were attached to the pupillary margin and obstructing the pupil so that effective pupil size was just 1 mm in mesopic state (Fig. 1A and B). The pupil was round, readily reacting to light and accommodation. During miosis, the lesions often obstructed the pupillary aperture. There were no signs of inflammation in the anterior chamber.

Examination with a Goldmann goniolens showed normal and open angular structures in both eyes. The fundus oculi were normal. Central corneal thickness was 507 µm in the right eye and 514 µm in the left eye. Intraocular pressure (IOP) was 10.7 mmHg in the right eye and 10.2 mmHg in the left eye. The visual acuity was 6/6 in both eyes without glasses. Anterior segment optical coherence tomography (AS-OCT) showed multiple cystic swellings at the pupillary margin with no peripheral cyst causing angle obstruction (Figs. 2 and 3). The patient was planned for Nd:Yag laser under topical proparacaine 0.5% in two sittings, 1 week apart, to avoid any reactive inflammation with energy of 0.5 to 1.2 mJ and two to three shots per cyst to rupture it. The cyst collapsed immediately as fluid oozed out, and the membrane wall of the cyst crumbled towards pupil margin increasing the effective size of the pupil (Fig. 4). There was no pain during the procedures. Post-laser, she was given topical loteprednol four times a day and timolol (0.5%) eye drops for a week. There was no recurrence of cyst till 5 months follow up and patient was asymptomatic even in bright light.

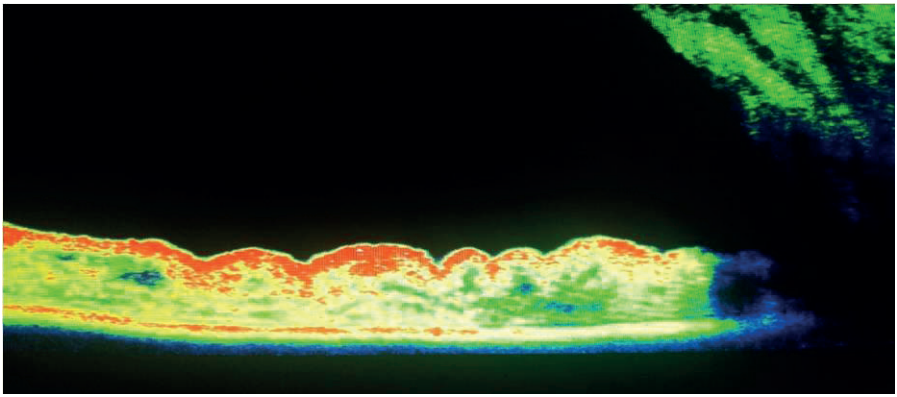

Fig. 2. AS-OCT showing iris pigment epithelial cysts at pupillary margin.

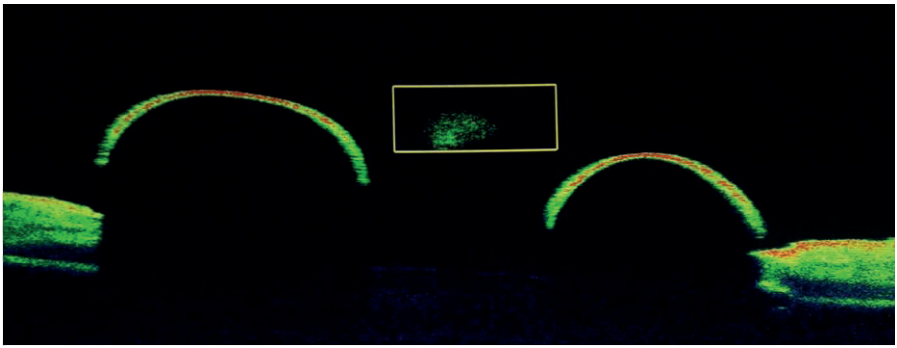

Fig. 3. AS-OCT showing no peripheral cyst causing angle obstruction.

Discussion

Primary iris cysts are found along the posterior surface of the iris, from the pupillary margin to the anterior ciliary body. Shields distinguishes four types, according to their position in relation to the iris: central, at the pupillary margin; midzonal, between the pupillary margin and the iris root; peripheral, at the irido-ciliary sulcus, and dislodged, in the anterior chamber or the vitreous cavity. The vast majority of them (76%) are peripheral. Most of them are stationary and small, and sometimes regress spontaneously. They are usually dark brown, round or oval with a thin wall and sonolucent contents.[1] The high reflectivity of their wall is attributed to the epithelial cells, while their sonolucent core is compatible with a fluid content.

The origin of primary central IPE cysts is not clear. Their appearance in early childhood in a few familial cases suggests that they may be hereditary with an

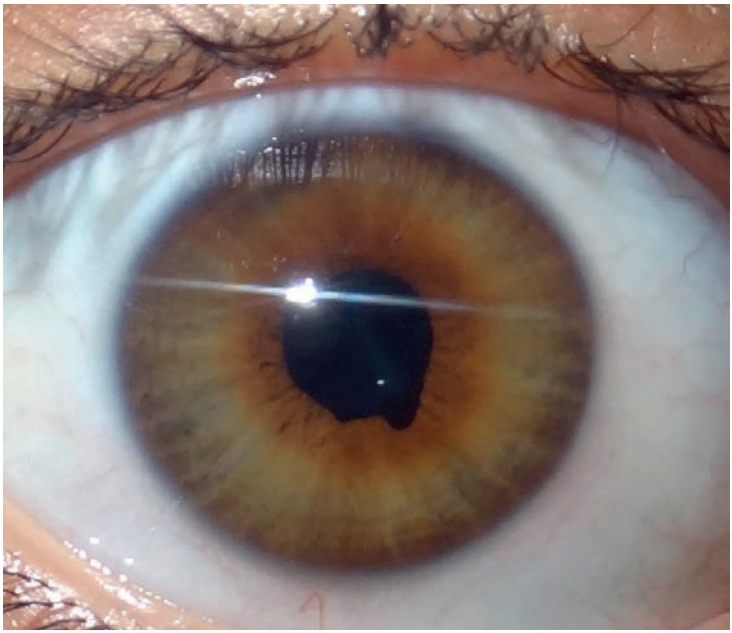

Fig. 4. Post-Nd:Yag laser rupture of three collapsed cysts resulting in clearing of the central visual axis.

autosomal dominant pattern.[2,3] Lewis et al. described an association with familial aortic dissection.[4] The proposed theory of formation of these cysts is traction of zonules on the anterior part of optic cup on ciliary epithelium at the fourth month of development. Histologically they are lined by pigmented epithelium and contain clear fluid. This patient neither had any associated systemic diseases nor did other members of her family have similar feature. Primary IPE cysts have often been misdiagnosed as iris or ciliary body melanoma.[5] Cysts of the iris are more likely to be confused with melanoma than those of ciliary body because of their pigmentation and more anterior location. It was believed that most primary IPE cysts are ophthalmic curiosities that need prolonged observation and no treatment.[1]

The natural course of primary epithelial cysts differs from that of secondary iris cysts, which follow surgical or non-surgical trauma. The latter lesions frequently enlarge and lead to severe complications such as inflammation and glaucoma. A steadily growing cyst, however, may disturb vision by covering the visual axis and provoke an increase in IOP or even inflammation if it touches the corneal endothelium. Their presence is occasionally responsible for plateau iris syndrome and secondary pigment dispersion syndrome.[2,3] Steps must then be taken to prevent

or treat complications, such as pupillary obstruction, secondary glaucoma, iridocyclitis, corneal decompensation and loss of vision. These cysts can be ruptured non-surgically by Nd:Yag laser as was done in this case, so that they do not interfere with vision or cause some visual-threatening situations in future.

Different treatment modalities have been suggested for management of these cysts. These include mitomycin C injection into the cyst and needle aspiration with endodiathermy, Nd:Yag laser cystotomy, excision of cysts and intracystic ethanol irrigation.[6-10] Risks of all treatment options include bleeding, endophthalmitis, cataract formation and cyst recurrence. Perhaps the most concerning risk in treating an epithelial inclusion cyst is the possibility of spilling epithelial cells outside the cyst, which could result in epithelial downgrowth.

We treated this case with Nd:Yag laser and the response was dramatic. The patient no longer complained of decreased field of vision in bright sunlight. No pigment dispersion or increase in IOP was seen 2 weeks post-laser. There is least possibility of recurrence of these cyst following Yag laser cystotomy, although multiple punctures are unlikely to close and pigment epithelial cyst remains stationary in size when untreated. But no recurrence was observed till 5 months follow up and patient was asymptomatic even in bright light. Thus, Nd:Yag laser is a successful modality for improvement of hemeralopia, providing cosmetic restoration and preventing further complications.

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Asian J Ophthalmol. 2020;17:10-18

Dacryocystorhinostomy for the treatment of nasolacrimal duct obstruction: a pilot trial to assess impact on coexisting sinus symptoms

Ankur Mehta[1,3], Wan Yi[1], Arjuna Ananda[2], Raf Ghabrial[1-3]
[1]Sydney Eye Hospital, Sydney, Australia; [2]Royal Prince Alfred Hospital, Sydney, Australia; [3]University of Sydney Medical School, Sydney, Australia

Abstract

Purpose: *To report on coexistent sinus symptoms in a population of patients who underwent endonasal dacryocystorhinostomy (DCR) surgery for nasolacrimal duct obstruction (NLDO) in a pilot study designed to test and refine methods and to estimate patient sample size for a larger multicentre randomised trial.*

Methods: *Ninety-four consecutive patients with NLDO who underwent endonasal DCR by three surgeons in both public and private practice over a two-year period were included in this study. Questionnaires were given preceding DCR surgery and at 10 weeks post-surgery. Sinus symptoms including sinusitis, nasal congestion, hyposmia, nasal discharge, and facial pressure were assessed in the questionnaire. All subjects underwent primary endonasal DCR and all patients underwent the same post-operative regimen.*

Results: *Questionnaire responses revealed that 48/94 (51%) patients had one or more sinus symptoms prior to DCR surgery. Ten-week post-DCR follow-up questionnaires were obtained from 77/94 (82%) patients. About 20/31 (65%) patients with one or more sinus symptoms prior to DCR surgery reported resolution of coexisting sinus symptoms by 10 weeks post-DCR surgery.*

Conclusion: *The data from this pilot study suggest that approximately half of patients attending for NLDO have coexisting sinus symptoms. There was some loss to follow-up. This pilot study highlighted the need for a validated patient questionnaire, longer length of follow-up, control groups for surgical intervention, and use of perioperative medications. Any clinical trial designed to assess the impact of endonasal surgery on sinus symptoms would need to enrol several hundred patients in order to reach a statistically valid conclusion.*

Keywords: *dacryocystorhinostomy, nasolacrimal duct obstruction, sinus symptoms*

Introduction

Nasolacrimal duct obstruction (NLDO) can cause epiphora, blurred vision, and recurrent superficial ocular infections.[1] Dacryocystorhinostomy (DCR) is the recognised standard surgical treatment for nasolacrimal obstruction.[1,2] External

Correspondence: Ankur Mehta, Sunder Eye Infirmary, Queen Alexander Rd, Sunderland SR2 9HP, UK.
E-mail: drankurmehta@outlook.com

or endonasal approaches for DCR are accepted as valid treatments for NLDO.[2] Our clinical experience has shown that patients attending the clinic with symptoms of NLDO have reported coexisting sinus symptoms. It has been shown that up to 70% of patients with NLDO have radiological evidence of sinus pathology[3], but there is a paucity of data reporting the subjective impact of sinus disease on patients presenting with NLDO.

Patient satisfaction and symptom relief are key outcome measures when assessing the success of surgical intervention. Patient questionnaires have been shown to be useful tools in measuring these outcomes.[1,4] The authors designed a questionnaire-based prospective pilot study to investigate the relationship between NLDO and sinus disease and to evaluate if surgical intervention for NLDO had an impact on the reported sinus symptoms.

Materials and methods

This prospective qualitative pilot study was made up of 94 participants from both private practice and quaternary referral hospital clinics. Three surgeons performed DCR surgery at three separate locations. All participants underwent primary endonasal DCR for NLDO. Surgical technique was similar between the three participating surgeons:

1. Incision in the lateral mucosa at the ridge above the base of the inferior turbinate, just lateral to the anterior lip of the middle turbinate at the level of the lacrimal sac, using a no. 11 blade.
2. Kerrison Rongeur was used to create the osteotomy.
3. Punctal probe inserted in inferior puncta and advanced into lacrimal sac.
4. Probe position used to identify lacrimal sac and visualised endonasally.
5. Incision and flap formation of lacrimal sac. Flaps reflected into nasal cavity opening.
6. Silicone tubal stents were inserted from the superior and inferior puncta and joined (by knotting) in the nasal cavity.
7. Stat triamcinolone (40 mg/ml in 1 ml preparation) was used post-stent insertion (one drop at the site of puncta).
8. The participants were advised to use topical chloramphenicol (1% in a 4 g preparation) ointment or drops for three days post-procedure.
9. Silicone tubal stents were removed at six weeks in an outpatient appointment.

A questionnaire was provided to all participants (Appendix 1). The questionnaire was based on the most common symptoms of sinus pathology. Participants were asked about previous history of sinusitis and previous sinus surgery. Specific sinus symptom history was recorded with regards to the following: nasal congestion,

post-nasal drip, nasal discharge, hyposmia, and facial pressure. Participants completed an identical questionnaire at 10 weeks post-surgery in a follow-up appointment. Patients who had initially reported coexisting sinus symptoms formed the cohort for evaluating any impact of DCR surgery.

Written informed consent was obtained from all participants. Ethics approval was obtained from the Human Research Ethics Committee—Northern Sector of the South Eastern Sydney Local Health District of NSW Health, Australia. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Results

Ninety-four subjects were recruited for prospective analysis prior to DCR surgery. Sixty two were female (66%). Forty-eight participants (51%) comprising 31 females (65%) reported one or more symptoms of sinusitis prior to DCR surgery. Some participants reported more than one sinus symptom.

The reported coexisting symptom was nasal congestion (35%), facial pressure (16%), nasal discharge (10%), and hyposmia (7%). Seventeen of these participants (18%) were lost to follow-up at 10 weeks (Table 1). By comparing the pre-surgery questionnaire with the post-operative questionnaire, a score of "improvement" was given if the symptom documented in the pre-operative questionnaire was omitted from the post-operative questionnaire. In cases where more than one sinus symptom was documented, scoring "improvement" was given if one of the sinus symptoms was omitted from the post-operative questionnaire. Of the 31 remaining participants who had reported pre-existing sinus symptoms, 20 (65%) reported improvement in their sinus symptoms following DCR surgery (Fig. 1).

Of the 46 participants who reported no symptoms of sinusitis prior to DCR surgery, none were lost to follow-up. Of these participants, no one reported onset of symptoms of sinusitis at 10-week follow-up.

Table 1. Sinus symptoms reported

Sinus symptoms	Totals	Total (%)
Nasal congestion	33	35
Facial pressure	15	16
Nasal discharge	9	10
Hyposmia	7	7

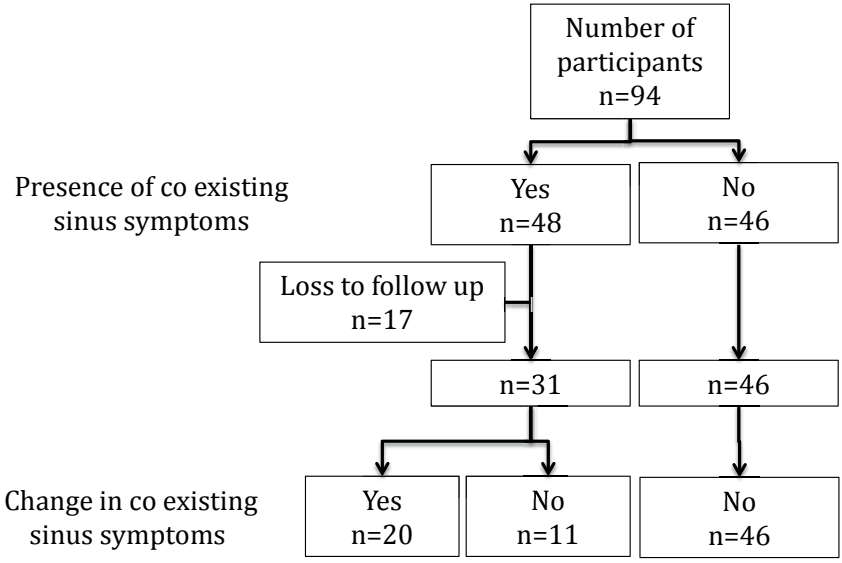

Fig. 1. Study design and outcomes.

Discussion

There is a paucity of data in the literature evaluating the relationship between the symptoms associated with sinus disease and the symptoms associated with NLDO. The aim of this pilot study was to identify if a relationship does exist and to give direction for further studies to evaluate this relationship. In this study, we found that 51% of patients who attended for endonasal DCR surgery for treatment of NLDO reported coexisting sinus symptoms. A study performed by Eyigor *et al*. reviewed 37 patients undergoing DCR surgery for NLDO. Paranasal computed tomography imaging showed that 73.3% had objective sinonasal abnormalities consistent with sinus disease. This suggests that there may be poor correlation between objective sinus disease (73.3%) and subjective symptoms of sinus disease (51%). Interestingly, the study reported a positive correlation between radiological evidence of sinus disease and NLDO and a lower success rate in treating NLDO with endonasal DCR in the cohort that had radiological evidence of sinus disease, and this may suggest a possible relationship between the two pathologies.[3]

The questionnaire used in this study was based on the common sinus-related symptoms (Appendix 1). Smirnov *et al.* trialled a novel scoring system to evaluate NLDO and endonasal DCR called the NLDO Symptom Score (NLDO-SS).[1]

Sixty-four patients were reviewed and their subjective responses were compared with a standardised, validated generic item measure of patient benefit called the Glasgow Benefit Inventory (GBI). They concluded that endonasal DCR improved quality of life when measured using the GBI and that their questionnaire correlated well with the GBI score and gave more information about the benefits after endonasal DCR than GBI alone.[1] Penttila *et al.* validated the NLDO-SS. They reviewed 86 eyes that underwent endonasal DCR and compared an objective outcome measure (irrigation of nasolacrimal apparatus) with the NLDO-SS qualitative outcome.[4] They reported that the NLDO-SS was a feasible clinical tool in measuring outcomes for endonasal DCR. The NLDO-SS asked for responses related to NLDO: tearing, discharge, swelling around the eyes, pain around the eyes, change in visual acuity, and included two further categories related to nasal symptoms: nose blockage and nasal cavity discharge. These criteria are similar to the questionnaire used in this study. The use of a validated questionnaire-based qualitative tool like the NLDO-SS would improve the interpretation of outcomes.

In this study, a standard 10-week follow-up was used to assess the outcome of endonasal DCR procedure. Solar *et al.* assessed 275 subjects by questionnaire at 3, 6, 12, and 18 months post-surgery and found that peak improvement was reported at 3 months[5], and Young *et al.*[6] reviewed 82 patients undergoing endoscopic sinus surgery for chronic sinusitis. In this group, a visual analogue score (VAS) was used to assess symptoms. The score was repeated at 3, 6, 12, 24, and 36 months. Analysis showed that the VAS score at 3 months was not statistically different to that VAS score at 36 months. This suggests that the optimal time to assess sinus symptoms post-surgery is at three months or 12 weeks. The two-week variation in assessment is a potential bias in this study, and its impact on the outcome is difficult to quantify.

In this study, we showed that 65% of patients who reported sinus symptoms pre-DCR reported improvement in their symptoms post-endonasal DCR. This may indicate a relationship between NLDO and sinus disease. The mechanism by which endonasal DCR may impact sinus disease is unclear.

Endonasal DCR uses instrumentation in the nasal cavity and intraoperative and post-operative medications. This raises the question if the surgical procedure itself or the medications used improves symptoms by changing the calibre of the nasal cavity or impacting in sinus disease, respectively. The authors could find no previous studies assessing the calibre of the nasal cavity pre- or post-endonasal sinus or DCR surgery. To assess for the impact of medications, a trial of the regimen used intra- and post-operatively on subjects presenting for NLDO surgery with coexisting sinus disease pre-surgery and assessing outcomes using a qualitative questionnaire is one option to control for this variable. The authors recognise this as a potential bias in this study.

The anatomical proximity of the nasolacrimal duct and the sinus system in the head and neck are well documented in ophthalmology anatomy text;[7] so it is reasonable to hypothesise that a pathological disease that is affecting one system could be involving the second.[3] Both structures are lined with mucosal tissue. The nasolacrimal duct is lined with goblet cells and intraepithelial mucus glands and has microvilli present;[8] the sinus systems are also lined with goblet cells but have ciliated pseudo-stratified epithelium cells instead; and these similar histopathological features reflect the similar defensive functions of the two structures.

Approximately half of the lymphocytes of the immune system are in mucosa-associated lymphoid tissue (MALT).[9] MALT tissue is present in the nasolacrimal duct, referred to as lacrimal duct-associated lymphoid tissue, and documented MALT-associated lymphomas have been reported in the paranasal sinus.[10] It has been shown that although MALT sites can be anatomically separated they remain functionally connected in what has been termed the common mucosal immune system.[11] This could suggest that an inflammatory response in the nasolacrimal duct could stimulate a similar response in the sinus system or vice versa, but in the absence of any evidence this remains purely speculative. Shams *et al.* reviewed 196 patients undergoing DCR.[12] Of the cohort, 20 subjects (10.2%) had chronic rhinosinusitis (CRS) and they found three of these (1.5%) developed acute rhinosinusitis (ARS), although all three were symptom free at the time of surgery. The authors suggest that CRS is a risk factor for developing ARS post-DCR. In their review, the authors discount surgical trauma or stent insertion as a cause for ARS (video review of surgical procedure and all three cases did not have stents inserted) and felt that perhaps either acquired or congenital narrow nasal space or nasociliary dysfunction secondary to CRS may have attributed to developing ARS. The mechanism for ARS post-DCR is unclear.

A limitation of our study was the loss to follow-up for 17 participants who had reported one or more sinus symptoms preceding DCR surgery.

Conclusion

These results indicate that a significant proportion of patients who attend for DCR surgery for the treatment of NLDO have coexisting subjective sinus symptoms. In this pilot study, we showed that the treatment of NLDO with endonasal DCR improved coexisting sinus symptoms in 65% of these patients. In this study, we found that a sample size greater that 385 would be needed in any clinical trial designed to evaluate the role of endonasal DCR surgery for NLDO on sinus disease to reach a statistically valid conclusion. This pilot study highlights the need for further studies in this area to further explore the relationship between sinus symptoms and NLDO and the potential treatment outcomes of endonasal DCR on coexisting sinus symptoms.

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PATIENT NAME: **DOB:** **PROCEDURE:** Dacryocystorhynostomy SYMPTOMS: **DATE OF PROCEDURE:** **DATE OF FOLLOW-UP:**		OPEN/ENDOSCOPIC (Please circle) LEFT/RIGHT (Please circle) Epiphora/Dacryocystitis
1. Previous history of sinusitis	Yes/No (Please circle)	
If yes, did sinusitis PRECEDE/CONTINUE/COME AFTER epiphora?		
2. Previous sinus surgery	Yes/No (Please circle) LEFT/RIGHT (Please circle)	
If **YES** to Question 1 &/or 2, answer the following questions:		
	PRE-PROCEDURE	**AT FOLLOW-UP (10 weeks)**
3. Nasal congestion	Yes/No	Yes/No
4. Post-nasal drip	Yes/No	Yes/No
5. Nasal discharge	Yes/No	Yes/No
6. Hyposmia	Yes/No	Yes/No
7. Facial pressure	Yes/No	Yes/No
	If **YES**, state **location** e.g. forehead, nasal or maxillary region:	
	If **YES**:	
	LEFT/RIGHT	LEFT/RIGHT

8. Epiphora	Yes/No	Yes/No
	If **YES**:	
	LEFT/RIGHT	LEFT/RIGHT
9. Regional symptoms *e.g.* cough, irritation, discomfort, change in taste, other symptoms		
ANY OTHER COMMENTS *e.g.* Peri-operative complications		

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Difference in prevalence of diabetes and diabetic retinopathy among low-altitude dwellers vs. high-altitude dwellers in North India

Anil Chauhan[1], Anil Kumar Verma[1], Deepak Sharma[1], Lalit Gupta[1], Dinesh Kumar[1], Gaurav Sharma[1], Ashoo Grover[2]

[1]Department of Ophthalmology, Dr Rajendra Prasad Government Medical College, Kangra, India; [2]Indian Council of Medical Research, New Delhi, India

Abstract

Background: *Type-2 diabetes mellitus (DM) is one of the leading lifestyle-related chronic disease as its prevalence is expected to rise up to 24.0% in the world by 2025, which was only 6.3% in year 2003.*

Objective: *To understand the high-altitude and low-altitude differentials for DM and diabetic retinopathy (DR) prevalence in a sub-Himalayan state of North India.*

Methods: *The study was carried out in the Shahpur block of Kangra district (altitude 2,404 feet) and the Spiti block of Lahaul and Spiti district (altitude 12,500 feet) of Himachal Pradesh.*

Results: *Among diabetics, the prevalence of DR was observed to be high (18.1%) in low landers and low (5.0%) in high landers. DM was more of a problem among low landers with a prevalence of 12.3% when compared to high landers (7.2%). Overall, the odd ratio of DR was twice as high (2.2; 95% confidence interval [CI]: 1.1-2.3) among patients with an unsatisfactory level of HbA1c (>8.0%) adjusted for gender, age group, smoking status and hypertension.*

Conclusion: *Differential did exist, as DM and DR were significantly lower in high-altitude areas when compared to low-altitude areas.*

Keywords: *diabetes mellitus, diabetic retinopathy, high landers and low landers, retinopathy*

Introduction

Type-2 diabetes mellitus (DM) is one of the leading lifestyle-related chronic diseases as its prevalence is expected to increase up to 24.0% globally by 2025 when compared to 6.3% in the year 2003: most in East Asia and Pacific and least in sub-Saharan Africa region.[1] Worldwide, DM causes estimated 9,59,000 deaths and 19,96,000 disability-adjusted life years.[1] DM-associated mortality and morbidity is due to micro-vascular

Correspondence: Dr Anil Chauhan, Professor, Department of Ophthalmology, Dr Rajendra Prasad Government Medical College, Kangra at Tanda, Himachal Pradesh 176001, India.
E-mail: dr.a.chauhan@gmail.com

(retinopathy, nephropathy and kidney failure) and macro-vascular (coronary heart disease, stroke, peripheral vascular disease and lower-extremity amputation) complications. Diabetic retinopathy (DR) is one of the serious complications, and if detected late can cause severe and irreversible loss of vision in an affected eye.

Lifestyle factors like physical inactivity, unhealthy diet, tobacco smoking and alcohol consumption are observed to be responsible for the onset of chronic diseases, including DM. Earlier considered only to be the disease of urban, chronic conditions have now been reported from rural areas of the country.[1-4] Evidence from population living in lower-altitude areas are available, but it is scanty for people living in high altitude. Therefore, present study was planned to assess the prevalence of DM and DR among low landers and high landers in a sub-Himalayan state of North India.

Methodology

This study was carried out in Shahpur block (low-altitude belt, 2,404 feet) of Kangra district and Spiti block (high-altitude belt, 12,500 feet) of Lahaul and Spiti district of Himachal Pradesh. This high-altitude belt is also the tribal belt which is a state notified area, and its population resides at an average of 12,500 feet from the mean sea level (MSL), whereas low-altitude areas spread over an average of 2,404 feet from the MSL. Population of tribal area residing in tough environmental conditions, as the area remained isolated from the rest of state due to heavy snowfall for 6 months (November to April), and inter-village connectivity remains disrupted for 3 months (December to February) every year. People living in the tribal area carry out agriculture, horticulture and cattle farming for livelihood. In order to estimate the prevalence of DM, the sample size of 3,445 in each area was calculated assuming 10.0% prevalence, design effect of 4, 80.0% study power and 95.0% level of significance. The villages were considered as the unit (cluster) of the study and 20 clusters with probability proportion to size were selected from the list of villages of each area. Structured interview schedule was administered by the trained field staff along with anthropometry and assessment for DM. It was done in the selected village across its entire households by door-to-door survey among individuals more than 20 years of age. Information on smoking, hypertension, duration of diabetes and family history of DM was collected along with the assessment for fasting blood sugar (FBG) with a standardized glucometer. Individuals with known case of DM and with FBG of ≥126 mg/dl were labelled as diabetics, and all of them were then assessed for glycosylated haemoglobin (HbA1c) with Nyco Card reader. All diabetics were assessed by an ophthalmologist for DR with the Fundus camera (VisuCam-500) along with measurement of intraocular pressure

(IOP) with the use of the tonometer. The informed consent was sought from the participants during the interview, anthropometry, blood sample collection and retinal assessment. The study was funded by the Indian Council of Medical Research, New Delhi, India, and approved by the Institute Ethics Committee. Data was entered and analyzed using the Epi Info software, Centre for Disease Control, Atlanta.

Results

Totally 2,204 individuals in the high-altitude area and 3,404 individuals in the low-altitude area were interviewed and assessed for DM. The prevalence of DM was found to be 7.2% among the high landers and 12.3% among the low landers with the mean FBG level of 101.1 mg/dl and 136.6 mg/dl in the high landers and low landers, respectively. The levels for the mean FBG was 104.9 mg/dl and 158.1 mg/dl in already known cases of DM. The prevalence of DR in the screened population was 0.3% among high landers and 2.2% among low landers. DR was prevalent in 5% and 18.1% of diabetic patients in the high-altitude and low-altitude areas, respectively (Table 1).

Looking for the differential variables, it was observed that the mean age of the screened population was 50.1 years in high landers when compared to 56.3 years in the low landers. The average age of diabetics in high landers was low (51.9 years) when compared to low landers (57.2 years). The age group distribution observed that more than half of the screened and about half of diabetic population were of 20 to 50 years of age in high-altitude area, indicating relatively more representation of younger population.

A gender differential was observed as significantly more proportion of males were screened (41.1% vs. 25.3%) and found diabetic (44.9% vs. 33.2%) in the high-altitude area when compared with the low-altitude area.

The prevalence of known cases of DM among all diabetics was 7.9% among the high landers and 84.4% among the low lander. Among known cases of DM, the regular intake of medicine was reported in 21.7% and 90.3% patients of the high-altitude and low-altitude areas, respectively (Table 1).

Among diabetics who reported history of regular intake of anti-diabetic drugs, the significant difference in the mean level of HbA1c was found to be 9.3 (SD ± 2.5) and 7.7 (SD ± 1.7) ($p < 0.0011$) among high landers and low landers, respectively. The prevalence of unsatisfactory levels of HbA1c (>8.0%) was observed to be 80.0% among high landers and 40.0% among low landers ($p = 0.05$) (data not shown). But when assessed for all diabetics (old and new), it was observed that the mean HbA1c was lower among high landers (6.3% vs. 7.7%) with relatively low prevalence for unsatisfactory levels of HbA1c (≥8.0%) among high landers (11.3% vs. 41.1%) when compared to the low landers (Table 2).

Table 1. Distribution of observed variables among screened population and diabetics in high-altitude and low-altitude areas of Himachal Pradesh, India

Variable	Screened population		P-value	Diabetics		P-value
	High landers (2,204)	Low landers (3,404)		High landers (159)	Low landers (418)	
Mean FBS (mg/dl) (±SD)	101.1 (28.3)	136.6 (65.9)	<0.001	104.9 (32.0)	158.1 (51.5)	<.001
Mean age (years) (± SD)	50.1 (10.9)	56.3 (11.3)	<0.001	51.9 (10.0)	57.2 (9.1)	<0.001
Age group (years) (%)						
20-40	26.5	6.9	<0.001	20.2	3.1	<0.001
41-50	35.9	32.3	<0.001	29.1	23.2	0.07
51-60	20.2	28.8	<0.001	30.1	43.7	<0.001
61-70	11.5	21.7	<0.001	16.4	23.4	0.02
>70	5.9	10.2	<0.001	4.1	6.7	0.14
Male (%)	41.1	25.3	<0.001	44.9	33.2	<0.001
Known case of DM (%)				7.9	84.4	<0.001
Family history of DM (%)				2.0	21.2	<0.001
Known case of hyperten-sion (%)				6.5	39.6	<0.001
Taking treatment for DM (%)				21.7	90.3	<0.001
Duration of smoking						

Variable	Screened population		P-value	Diabetics		P-value
	High landers (2,204)	Low landers (3,404)		High landers (159)	Low landers (418)	
<1 year	4.0	2.0	<0.001[a]	2.9	0.0	NA
1-5 year	10.3	7.0	0.13	2.9	2.0	0.01
5-10 year	14.3	2.6	<0.001	20.6	5.9	0.08
>10 year	71.3	95.5	<0.001	73.5	92.2	0.01
Cigarettes per day						
<5	17.8	21.5	0.28	11.8	27.5	0.08
5-10	13.0	19.4	0.04	8.8	13.7	0.73[a]
>10	68.9	58.8	0.01	79.4	58.8	0.04
Ever tested for lipids (%)	0.5	16.6				
Mean blood pressure	127/34	128/78	<0.001	126/88	134/88	<0.001
hyperten-sion stage (mmHg)						
Normal (<120 and <80)	42.8	41.4	<0.001	33.2	39.1	0.13
Pre (120-139 or 80-89)	37.3	39.7	<0.001	19.9	20.3	0.87
Stage-1 (140-159 or 90-99)	12.3	16.9	<0.001	28.4	31.3	0.42
Stage-2 (≥160 or ≥100)	7.6	2.9	<0.001	18.5	9.3	<0.001

[a]Yates' corrected Chi-square

Table 2. Distribution of fasting blood sugar, HbA1c and IOP detected in diabetics and individuals with DR in high-altitude and low-altitude areas of Himachal Pradesh, India

Variable	Diabetics		P-value	Diabetics with DR		P-value
	High landers (159)	Low landers (418)		High landers (8)	Low landers (76)	
Mean FBS (mg/dl) (±SD)	104.9 (32.0)	158.1 (51.5)	<0.001	146.8 (34.4)	185.6 (42.4)	0.12
HbA1C (%) (±SD)	6.3 (1.5)	7.7 (1.7)	<0.001	8.1 (2.0)	8.3 (1.7)	0.82
IOP right (±SD), mmHg	15.8 (4.1)	15.3 (4.3)	0.18	17.8 (4.8)	15.2 (4.1)	0.18
IOP left (±SD), mmHg	15.4 (3.9)	15.5 (4.5)	0.59	17.1 (3.0)	15.7 (4.6)	0.26
High HbA1c (>8.0%)	11.3	41.1	<0.001	66.7	62.2	0.82
Hypertension (Stage-1 and Stage-2) (%)	48.6	40.4	0.95	37.5	47.4	0.85

Among all screened for DM, an assessment for hypertension was performed, finding that the, prevalence of pre-hypertension and stage-1 hypertension was significantly high among low landers, whereas stage-2 hypertension was found to be high among high landers. Among diabetics, a similar but insignificant differential, was observed (Table 1).

Among high landers, the prevalence of smoking was 8.5% when compared to 11.8% among low landers ($p < 0.001$) with a smoking history for more than 10 years in about 71.3% of high landers and 95.5% of low landers ($p < 0.001$) (Table 1). Statistical insignificant difference was observed for IOP in both eyes (right: 15.8 vs. 15.3; left: 15.4 vs.15.5) between both areas (Table 1).

As the prevalence of DR was observed to be significantly high among low landers when compared to high landers and the number of DR cases was less in high-altitude area, so a statistically insignificant difference was observed for mean FBS, HbA1c, IOP and individuals with high HbA1c when compared to the low-altitude area (Table 2). Looking for the potential variables for the difference, it was observed that a significant odds ratio (OR) was observed for unsatisfactory

HbA1c levels among diabetics with OR of 19.8 (95% [confidence interval] CI: 3.3-118.2) in high altitude and 2.8 (95% CI: 1.7-4.8) in the low altitude. It was insignificant for gender, age group, smoking and hypertension. The wide CI was observed in high-altitude area because of relatively fewer number of DR cases (8). Therefore, combining all the cases of DR of both areas for assessment we observed that the OR of DR was significantly high among diabetics with high HbA1c, 4.3 (95% CI: 2.6-7.0) and individuals of 61 to 70 years of age, 1.8 (95% CI: 1.1-3.1). Looking for OR across the age group, an insignificant increasing risk from low to high age group was observed. Adjusting for factors like gender, age group, long duration of DM (high HbA1c), smoking and hypertension, it was found that the high HbA1c was associated with DR with an OR of 2.2 (95% CI: 1.2-2.7). It indicates that DR was approximately twice as high among diabetics with long duration of uncontrolled DM (Table 3). All the observed cases of DR were non-proliferative type and not even a single case of proliferative DR was observed in the present study. The most common observation for non-proliferative DR (NPDR) were haemorrhages,

Table 3. Unadjusted and adjusted risk assessment for DR in high-altitude and low-altitude areas of Himachal Pradesh, India

Variable	High landers (8)	Low landers (76)	Both (84)	
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Male	3.8 (0.7-19.2)	1.3 (0.7-2.1)	1.1 (0.7-1.8)	0.9 (0.5-1.6)
Age group in years (%)				
20-40	0.3 (0.0-4.6)	1.3 (0.3-5.0)	0.4 (0.1-1.1)	Constant
41-50	1.4 (0.3-6.3)	0.3 (0.1-0.6)	0.3 (0.1-0.7)	1.6 (0.4-6.6)
51-60	0.7 (0.1-3.8)	1.1 (0.7-1.8)	1.3 (0.8-2.0)	0.7 (0.2-2.6)
61-70	0.7 (0.0-5.9)	1.8 (1.0-3.1)	1.8 (1.1-3.1)	0.3 (0.0-1.3)
>70	3.5 (0.4-31.3)	1.2 (0.5-3.1)	1.6 (0.7-3.8)	0.3 (0.0-1.6)
High HbA1c	19.8 (3.3-118.2)	2.8 (1.7-4.8)	4.3 (2.6-7.0)	2.2 (1.1-2.7)
Smoker	1.2 (0.1-10.1)	1.1 (0.5-2.3)	1.1 (0.6-2.3)	1.0 (0.4-2.3)
Hypertension (Stage-1 & Stage-2)	0.6 (0.1-2.8)	1.4 (0.8-2.3)	1.1 (0.7-1.8)	0.7 (0.4-1.1)

CI: confidence interval; OR: odds ratio

microaneurysms and hard exudates. It was followed with fewer frequent findings of haze, torturous vessels, cotton wool spots and optic disc changes.

Discussion

DR is the most important cause of irreversible loss of vision. India is considered as diabetic capital of the World. Among diabetics, studies observed the prevalence of DR as 18% (CURES)[5] and 19% (APEDS),[6] 10.0%[7] and 21.6%.[8] Current study observed that among diabetics, the prevalence of DR was 18.1% in low-altitude areas and 5% in high-altitude areas. It was of NPDR in nature with significant differential distribution in studied areas. Among screened individuals, it was 2.2% among low landers and 0.3% among high landers. In general population of rural India, the prevalence of DR was observed to be 0.6%, 1.2%, 1.7%, which is quite similar to the present study.[8-10] However, in evidence from rural Bangladesh, DR prevalence was 5.4% in its studied participants.[11] As in the current study, NPDR was the common form in the rural area of Andhra Pradesh (96.4%).[11] DR is dependent on the duration of disease and its treatment, which is an important factor related to DM. The current study observed that the OR of DR was twice as high (2.2; 95% CI: 1.1-2.3) among patients with an unsatisfactory level of HbA1c (>8.0%) adjusted for gender, age group, smoking status and hypertension. As the biological plausibility, the long duration of DM is certainly the risk factor for DR in both the areas.

DM affects people of all ages and races with increasing prevalence worldwide. In certain regions, successive growth and development leads to associated lifestyle changes exemplified by the reduction of physical activity and increased consumption of high-energy processed foods.[12-14] DM prevalence in India ranged from 5.9% to 12.1% (North: 8.6%–11.6%; South: 13.5%–19.5%).[15,16] High prevalence of DM was observed both in urban and rural India (about 2.0%–10.0%),[16] whereas a systematic review for DM in tribal populations of India observed a ranging prevalence from 0.7% to 10.0%, with a final estimate of 5.9%.[17] The present study tends to understand the pattern of DM and DR as its complication among low landers and high landers. In the high-altitude area with limited availability and accessibility of health care resources, different lifestyle and poor network connectivity, an assumption for low risk for DM and DR was made in the current study. It was observed that the prevalence of DM was statistically high among low landers (12.3%) when compared to high landers (7.2%) ($p < 0.001$) with the high mean level of FBG among low landers (136.6 mg/dl) than high landers (101.1 mg/dl) areas. In the present study, about 60.0% among high landers and 40.0% among low landers were observed to be below 50 years of age, reflecting more of population with young age in high-altitude area when compared to low-altitude area. Among diabetics, about half of patients among high landers and about a quarter among low landers were below 50 years of age. Such type of supportive evidence was observed where about more than half of DM cases were

less than 50 years of age.[18] The high-altitude area (tribal area) in the current study was observed to have less prevalence for DM, which is in the observed range of evidence across the country. It may not be actually less but could be a marker for early appearance of chronic diseases in the tribal area.

Smoking increases the risk for DM and associated macro- and micro-vascular complications.[19,20] Smoking was found to cause substantial changes in insulin sensitivity among patients with non-insulin DM. A meta-analysis showed the prevalence of smoking was high among diabetic patients when compared to normal subjects.[21] Local evidence from a study conducted in the same state but in a different study area, observed that the prevalence of smoking among diabetics was about 10.0% in the urban and 4.0% in the tribal population.[22] The current study observed that among screened individuals for DM, there was low prevalence of smoking (8.5%) among high landers when compared to low landers (11.8%) ($p < 0.001$), but it was observed almost similar (about 10.0%-12.0%) among diabetics in both areas. However, in the low-altitude areas, significantly more screened individuals and diabetics were observed with smoking duration of more than 10 years and consumption of more than 10 cigarettes per day.

Hypertension is a common chronic morbidity associated with DM.[23] In India, the overall prevalence of hypertension is about 40.0%, more in urban (63.2%) than in rural (36.8%) areas and reportedly varies from 20.0% to 40.0% in urban and from 12.0% to 17.0% in rural India.[23] Hypertension and DM were observed as co-morbid conditions in a hospital-based study, as in diabetics hypertension prevalence was 60.2%, 76.5%, and 85.8% at blood pressure thresholds of 140/90, 130/85, and 130/80 mmHg, respectively.[24] Descriptive evidence from 10 states in India observed co-existence of DM and hypertension in 20.6% patients.[25] Another study from the same study area observed the prevalence of DM as 10.4% in stage-1 and 16.9% in stage-2 hypertension.[22] The current study observed that among all screened, hypertension was more prevalent among low landers: high prevalence of stage-1 hypertension among high landers and stage-2 hypertension among low landers. Among diabetics, the prevalence of stage-1 hypertension was found to be high in both areas, but stage-2 hypertension was significantly high in the high-altitude area. Overall, about 20.0% of the screened individuals were hypertensive, which is quite similar to study from central India that found hypertension in 19.4% of the population, but high when compared to 14.5% in the rural area of South India.

Surveys in developing countries suggest an early increase in the risks for chronic diseases like DM and hypertension.[26] The current study observed that there was high prevalence of hypertension, DM and DR among low landers in comparison to high landers, and being in the low-altitude area the OR for DM, hypertension and DR was twice as high than that of the high-altitude area. Evidence from Africa, China and the Pacific islands also documents that the risk-factor level increases when

people migrate to more urbanized settings.[21-25] In the present study, the degree of urbanization was not studied, but subjective, not objective, assessment of both the areas showed less urbanization in the high-altitude area when compared to the low-altitude area, which could be the reason for the observed differentials. The high-altitude area remains disconnected from the rest of the state in absence of rail, road and air transport, so, in itself it can be seen as a justification for the complete absence of urbanization. For the high-altitude area, though there was low prevalence of DR and relatively less prevalence for DM and HTN, the effect of urbanization in the coming times cannot be underestimated. So, it becomes important to establish an effective surveillance system to track the lifestyle changes within the community and measures to reduce the impact of urbanization.

There are limitations to the study, as the extent of urbanization was not studied objectively, and inferences drawn in the present evidence are based on the cross-sectional study. However, an effort was made to draw sufficient sample size in both areas to meet statistical assumption, although logistic regression was used as a multivariate statistical test which is robust to violation of assumptions. A far lower number of DR cases limits the statistical analysis, but there is sufficient evidence in favour of early onset of DM among high landers for regular screening and lifestyle interventions.

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Adult gonococcal keratoconjunctivitis: early detection is key

Daniel Lai[1], Keith Ong[1,2,3,4]

[1]Department of Ophthalmology, Northern Clinical School, University of Sydney, Sydney, Australia; [2]Department of Ophthalmology, Royal North Shore Hospital, Sydney, Australia; [3]Department of Ophthalmology, Sydney Adventist Hospital, Sydney, Australia; [4]Department of Ophthalmology, Chatswood Private Hospital, Sydney Australia

Abstract

We describe a case of a 52-year-old male presenting with severe mucopurulent conjunctivitis of the right eye. Corneal ulceration and associated anterior chamber activity was noted later in the course of the disease. Neisseria gonorrhoeae was positive on polymerase chain reaction (PCR) testing earlier than traditional microscopy and culture. He was successfully treated with ceftriaxone 500 mg intravenously and azithromycin 1 g orally as single doses in addition to ofloxacin ophthalmic solution 0.3% hourly to the right eye. This case highlights the need to consider the possibility of gonococcus in cases of suspected bacterial conjunctivitis, careful monitoring for corneal involvement and the importance of early detection with PCR.

Keywords: *corneal perforation, gonococcal conjunctivitis, Neisseria gonorrhoeae*

Introduction

Gonococcal conjunctivitis (GC) typically presents as a severe mucopurulent conjunctivitis with associated lid oedema, tenderness and often preauricular lymphadenopathy.[1,2] GC may be complicated by uveitis and severe keratitis. Variable corneal findings have been described, including subepithelial and/or stromal infiltrates, marginal corneal melt and diffuse oedema.[1,3] This is due to the fact that *Neisseria gonorrhoeae* is able to penetrate an intact cornea, causing aggressive invasion and poses a high risk of corneal perforation, reportedly within 24 hours of infection.[3,4]

As gonococcal infection in the eye is relatively rare, diagnosis can be delayed.[5] However, clinical outcomes are known to be related to severity of disease at the commencement of adequate therapy, thereby highlighting the importance of prompt diagnosis.[1]

We describe a case of adult GC with corneal involvement.

Correspondence: Daniel Lai, 38 Meredith St, Strathfield, NSW 2135, Australia.
E-mail: daniel.lai01@hotmail.com

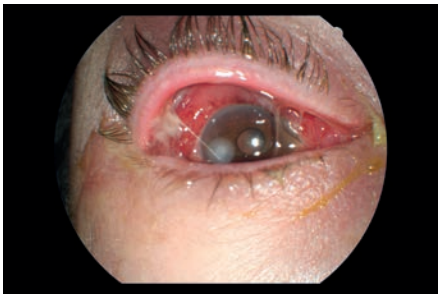

Fig. 1. Anterior segment photograph of the patient's right eye on presentation with intense conjunctival hyperaemia, chemosis and mucopurulent discharge apparent (day 1).

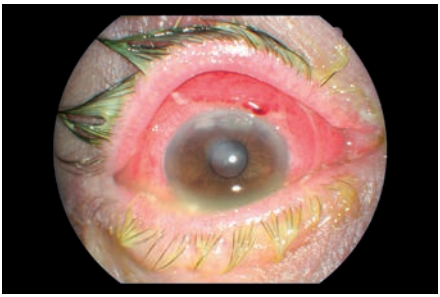

Fig. 2. Two infiltrates with overlying ulceration developing in the superior peripheral cornea evident two days later (day 3).

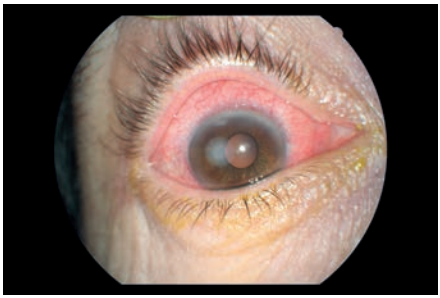

Fig. 3. Conjunctival inflammation and cornea infiltrates improving (day 5).

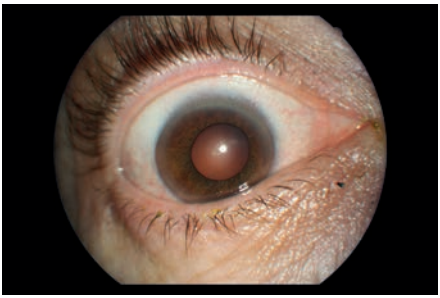

Fig. 4. Complete resolution (4 months).

Case report

The of face a 52-year-old male mechanic came into contact with debris while repairing a garbage truck. Two days later, he developed a painful eye associated with discharge and was put on chloramphenicol eye drops. His symptoms worsened and was referred to an ophthalmologist three days after the onset of his symptoms. Visual acuity was 6/60 in the right eye and 6/9 in the left eye; poor visual acuity was due to mucopurulent discharge and he could hardly open his right eye. On examination, there was significant inflammation of his right conjunctiva and upper eyelid with sloughing of the conjunctival epithelium epithelium (Figs. 1 and 2). The cornea was otherwise clear and anterior chamber was quiet. Conjunctival swabs were taken for microscopy, culture and sensitivity (MCS) and polymerase chain reaction (PCR) tests. A possible allergy to topical chloramphenicol was considered and his therapy was changed to oral doxycycline 100 mg daily.

When reviewed two days later, his conjunctiva and eyelid were less oedematous. However, two small areas of corneal infiltrates with overlying ulceration had developed in his superior peripheral cornea and inflammatory cells were noted in his anterior chamber (Fig. 3). He was subsequently placed on hourly ofloxacin 0.3% ophthalmic solution (Ocuflox, Allergan).

Microscopy revealed 2+ Gram-positive cocci and 3+ leucocytes. *Neisseria gonorrhoeae* was positive on PCR and there was light growth on culture. Sensitivities were not provided by the laboratory. He was given azithromycin 1 g orally as single dose on day 4. Due to difficulties in acquiring the medication, ceftriaxone 500 mg intravenously was administered the following day at a local hospital. On review, the corneal infiltrates and conjunctival inflammation showed significant improvement. The patient had no urethral symptoms and his partner underwent subsequent screening for sexually transmitted infections, which turned to be negative.

By day 24, the corneal infiltrates and ulcer had resolved, with only a faint residual haze in the superior cornea and his visual acuity improved to 6/9. Complete resolution was seen four months after initial presentation (Fig. 4).

Discussion

GC can be divided into two subsets: of those affecting the adults and of those affecting the neonates, with infection traditionally considered rare in adults.[5] In recent years, the incidence of gonococcal infection in Australia has increased by 118%, from 35.8 per 100,000 in 2005 to 78 per 100,000 in 2015.[6,7] This reflects trends in the developed countries, including England and Ireland, where GC is presenting more commonly in young adults with male predominance.[8]

The source of the infection in this case is unclear. While most infections occur as a result of sexual contact, GC is a highly contagious condition that has several other modes of transmission. Small numbers of sporadic cases in children or adults occur every year as a result of auto-inoculation in a person with genital gonorrhoea.[8,9] GC can also be transmitted by direct, non-intimate interpersonal contact or contact with infected fomites (e.g. clothes, towels).[9] The Australian bushfly (*Musca vetustissima* Walker*)* has also been implicated as a vector of infection.[10] More rarely, epidemics can occur within a remote community or over several communities and may involve dozens or even hundreds of cases. This has occurred in central Australia four times in the past 25 years.[11] Any new diagnosis raises the possibility of an epidemic occurring. Urgent notification is required, and investigation of the circumstances with a public health response is essential. Sporadic cases in children raise the possibility of sexual abuse and should be considered in patients aged less than 16 years.

Despite the well-described clinical features, incidence of gonococcal eye disease is still relatively low, leading to misdiagnosis. In one case series, all the cases of

corneal perforation secondary to gonococcal infection were initially attributed to epidemic keratoconjunctivitis.[12] Certainly in this example, a severe acute bacterial conjunctivitis, chloramphenicol allergy or chemical burn was initially considered with GC not routinely suspected. Therefore, conjunctival swabs were taken for routine MCS screening. *Neisseria gonorrhoeae* can be demonstrated by the presence of Gram-negative diplococci intracellularly.[13] However, given that the majority of bacterial conjunctivitis are self-limiting, it may not be feasible to obtain conjunctival swabs on all cases of conjunctivitis.[14] Indeed, guidelines dictate that conjunctival cultures should be reserved for suspicious cases.[15] Interestingly, microscopy revealed Gram-positive cocci in this case, highlighting the significance of confirmatory tests.

Nucleic acid amplification tests (NAATs) such as PCR amplify and detect nucleic acid sequences that are specific for a particular organism.[16] In theory, NAATs can produce a positive signal from as little as a single copy of the target deoxyribonucleic acid or ribonucleic acid, which makes NAATs extremely sensitive tests that decreases the time required to identify a pathogen. As such, PCR is now considered the gold standard for diagnosing GC.[17] Microbiology laboratories are often inundated with specimens, and when considering that remuneration is largely government funded in Australia, cost-effectiveness is of high consideration. One such measure that would allow definitive detection could be to have a system incorporating routine PCR alongside MCS.

Current Center for Disease Control and Prevention (CDC) recommendations for uncomplicated urogenital, anorectal and pharyngeal gonorrhoea propose combination antibiotic therapy with a single dose of ceftriaxone 1 g intramuscularly in addition to a single dose of azithromycin 1 g orally or doxycycline 100 mg twice daily orally for 7 days as presumptive treatment for concurrent *Chlamydia trachomatis* infection.[18]

Although not essential in the management of gonococcal ophthalmia, adjuvant treatment with saline lavage and topical antibiotics have been proposed.[19] Topical ofloxacin 0.3% was used in this case as we strongly believe that topical therapy should be used particularly in cases of corneal involvement.

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Fuchs endothelial corneal dystrophy and small eyes

Nicole Shao-Yuen Lim,[1] John Males[2]
[1]Department of Ophthalmology, Sydney Eye Hospital, Sydney, Australia; [2]The University of Sydney, Save Sight Institute, Sydney Eye Hospital, Sydney, Australia

Abstract

Aim: *To determine whether there is an association between Fuchs endothelial corneal dystrophy (FECD) and shorter axial length (AL), shallower anterior chamber depth (ACD) and higher spherical equivalent (SE). In addition, to evaluate whether there is a correlation between AL and severity of corneal decompensation in FECD, using corneal thickness as a proxy.*

Design: *Retrospective cohort study.*

Methods: *This was a single-centre study conducted in a cornea clinic in Sydney, Australia. Detailed clinical measurements of 91 eyes of 50 FECD patients were compared with 110 eyes of 55 controls. Main outcome measures included AL, ACD and SE. Other outcome measures included central corneal thickness, visual acuity, intraocular pressure and keratometry.*

Results: *Mean AL of FECD patients was 23.6 mm (standard deviation [SD] ±0.9 mm), compared with 24.7 mm (SD ±1.8 mm) for controls (1.1 mm difference [95% confidence interval [CI] 0.5-1.6], $p < 0.001$, independent sample t-test); corresponding means for ACD were 3.0 and 3.3 mm (0.32 mm difference [95%CI 0.2-0.5], $p < 0.001$, independent t-test). Eleven out of the 22 FECD patients with available refraction data had hypermetropic refraction compared with 16 out of 36 controls ($p = 0.68$, chi-squared test). The mean SE of FECD patients (+0.10D) was higher than controls (−1.33D) (1.4D difference [0.1-2.8], $p = 0.04$, independent t-test). No statistically significant correlation was found between AL and corneal thickness ($p = 0.28$, linear regression).*

Conclusion: *In this retrospective cohort study, a strong association was established between FECD and small eyes, with shorter AL and shallower ACD, compared with controls. These results have important implications for surgical planning, as shorter AL and ACD in FECD patients likely contribute to their high risk of corneal decompensation following cataract surgery.*

Keywords: *anterior chamber depth, axial length, Fuchs endothelial corneal dystrophy, hypermetropia, hyperopia*

Correspondence: John Males, Save Sight Institute, Sydney Eye Hospital, Level 12 Park House, 187 Macquarie St, Sydney NSW 2000, Australia.
E-mail: john.males@sydney.edu.au

Introduction

Fuchs endothelial corneal dystrophy (FECD) is the most common corneal dystrophy and one of the leading indications for corneal transplant.[1,2] The condition is characterized by progressive loss of endothelial cells and increase in extracellular matrix deposition at the level of Descemet's membrane.[3] Although the condition has been well defined clinically, refractive profiles and axial lengths (ALs) of patients with FECD have yet to be adequately described.

Only two small reports have attempted this. The first was a study of 24 patients by Pitts and Jay,[4] which suggested a tendency of FECD patients to be hypermetropic with short ALs. This was supported by a non-comparative series of 23 patients by Lowenstein et al.[5] Drawbacks of this research, published over two decades ago, include the small sample size, inclusion of measurements taken post-transplant and significant proportion of subjects excluded from analysis due to absent data. These studies also used applanation ultrasound biometry for AL and anterior chamber depth (ACD) measurements. Non-contact optical biometry has since surpassed ultrasonography as the gold standard technique for biometric parameters, facilitating more accurate and reproducible measurements.[6,7] Specifically, optical biometry has been found to be superior in eyes with short ALs, where there is potential for corneal compression with applanation ultrasound.[8]

Beyond these two studies, data characterizing refractive and AL profiles in patients with FECD is scarce, and to our knowledge, no study has documented ALs in FECD patients using optical biometry. As such, the purpose of this study is to investigate the association between FECD and axial hypermetropia and examine whether a correlation exists between shorter ALs and corneal decompensation. In doing so, we hope to contribute more extensive and precise data to better characterize these clinical profiles.

Materials and methods

In this retrospective cohort study, selection involved 51 consecutive patients with FECD who underwent Descemet's stripping endothelial keratoplasty or penetrating keratoplasty, combined with cataract removal by a single corneal surgeon (JM), based at a cornea clinic in Sydney, Australia between July 2010 and March 2014. Controls were 58 patients randomly selected from those undergoing cataract surgery alone, by the same surgeon (JM), throughout the same duration of time as the FECD cohort. A process of simple random selection was used by compiling and numbering a list of all cataract surgeries between July 2010 and March 2014, and using a random number generator software. Patients with FECD or other corneal pathology were excluded from the control cohort. The study adhered to the tenets of the Declaration of Helsinki.

Eleven eyes of nine patients in the FECD group and 10 eyes of 5 patients in the control group were excluded from analysis due to history of previous corneal

transplant, previous cataract surgery or inadequate data. The remaining 91 eyes of 50 patients with FECD and 110 eyes of 55 controls were included for analysis.

Medical records were reviewed, including preoperative clinical notes, optical biometry results, pentacam results and operation report. No postoperative data was utilized. Averages of measurements from both eyes were used for analysis.

The main outcome measures included AL, ACD and spherical equivalent (SE). AL and ACD measurements were obtained from optical biometry (IOLMaster, Carl Zeiss Meditec, Dublin, CA, USA). If possible, SE was calculated using whichever parameters for refraction were available in the clinical notes, which included a mixture of subjective and auto-refraction. Other outcome measures included central corneal thickness (thinnest), uncorrected visual acuity, intraocular pressure (IOP) and keratometry.

Statistical analysis was performed using the SPSS software, version 22.0 (IBM/SPSS Inc., Chicago, IL, USA). Independent sample t-tests were used to compare AL, ACD and SE. Chi-squared test was used to compare proportions of hypermetropic SE in each group. Simple linear regression analysis was used to correlate AL and corneal thickness.

Results

This study compared preoperative clinical measurements of 91 eyes of 50 FECD patients with 110 eyes of 55 controls. The baseline patient demographic is shown in Table 1. There was no difference in baseline age (69.6 vs 66.9 years, $p > 0.05$) or keratometry (43.66 vs 43.09, $p > 0.05$). The FECD group had a greater proportion of females (70% vs 53%), more astigmatism (1.67D vs 1.02D, $p < 0.01$) and lower uncorrected visual acuities (1.14 vs 0.89, $p < 0.01$) compared with controls.

Mean, standard deviation (SD) and confidence intervals (CIs) for AL, ACD and SE are presented in Table 2. Strong evidence of an association was found between FECD and AL. The mean AL of FECD patients (23.6 mm SD ±0.86) was lower than controls (24.7 mm SD ±1.76), with a mean difference of 1.1 mm (95% CI [0.57-1.63 mm]) ($t = 4.12$ with 81 degrees of freedom [df], $p < 0.001$, independent sample t-test).

FECD patients were also found to have shallower ACD. The mean ACD of FECD patients (3.0 mm SD ±0.5) was shorter than controls (3.3 mm SD ±0.4), with a difference of 0.32 mm (95% CI [0.17-0.50]) ($t = 3.79$ with 101 df, $p < 0.001$, independent sample t-test).

Refractive data was available for 22 FECD patients and 36 controls. Of these, 11 FECD patients (50%) had hypermetropic refraction with a mean SE of +1.40D (SD ±0.86); 16 controls (44%) had hypermetropic refraction. Although the proportion was higher in the FECD group, this was not statistically significant ($\chi^2 = 0.17$ with 1df, $p = 0.68$, chi-squared test). The overall mean SE of FECD patients (+0.10D

Table 1. Comparison of baseline characteristics between FECD and control groups

Variable	FECD mean (n = 50)	Control mean (n = 55)	P-value[a]
Age (years)	69.6	66.9	0.21
Sex Female Male	 35 (70%) 15 (30%)	 29 (53%) 26 (47%)	
LogMAR VA (95% CI)	1.14 (0.98-1.30)	0.89 (0.76-1.02)	<0.01
Keratometry (95% CI)	43.66 (43.19-44.13)	43.09 (42.53-43.65)	0.27
Astigmatism (95% CI)	1.67 (1.31-2.02)	1.02 (0.85-1.18)	<0.01
IOP (95% CI)	14.1 (13.1-15.1)	15.4 (14.3-16.4)	<0.01

[a]Independent sample t-test

Table 2. Comparison of AL, ACD and SE between FECD and control groups

Variable	FECD mean	Control mean	Mean difference [95% CI]	P value[a]
AL (mm)	23.6 ± 0.9 (n = 49)	24.7 ± 1.8 (n = 55)	1.1 [0.5-1.6]	0.001
ACD (mm)	3.0 ± 0.5 (n = 48)	3.3 ± 0.4 (n = 55)	0.32 [0.2-0.5]	0.001
SE (D)	+0.1 ±1.6 (n = 22)	−1.3 ± 3.5 (n = 36)	1.4 [0.1-2.8]	0.036

[a]Independent sample t-test

SD ±1.57) was higher than controls (−1.13D SD ±3.45), with a statistically significant difference of 1.43D (95% CI [−0.09 to 2.76]) (t = 2.15 with 53df, p = 0.036, independent sample t-test).

No statistically significant correlation was found between AL and corneal thickness (R^2 = 0.2%, β = −3.72; p = 0.28, simple linear regression).

Discussion

With the use of non-contact imaging techniques, this study has provided strong evidence that patients with FECD have smaller than average eyes, with shorter AL and shallower ACD than controls. The main implication of these results is that

shorter AL and ACD in FECD patients likely compound their risk of endothelial decompensation following phacoemulsification cataract surgery.

This is based on the premise that a shorter distance between ultrasound energy and the endothelium makes eyes more vulnerable to endothelial cell loss due to the closer proximity of heat and ultrasound energy, as well as movement of lens fragments and the risk of touch from surgical instruments.[9] As such, shorter ACD and AL have been established as poor prognostic factors leading to greater endothelial cell loss as per Hwang *et al.*[9] and Walkow *et al.*[10] This underscores the importance of surgical planning and risk in FECD patients.

The refractive outcomes of this study were unfortunately less conclusive than our AL and ACD results, with a statistically higher mean SE in FECD group, yet no statistically significant difference in prevalence of refractive hypermetropia between groups. These results may be confounded by the presence of cataract, as increasing severity of cataract is known to induce myopic shift.[11]

The demographic profile of our cataract cohort seems to be consistent with data from previous large population-based cataract studies, in terms of age and the male-to-female ratio.[12,13] Average AL in these cataract cohorts vary, with some reasonably shorter (23.89 ± 1.77 [12]) than ours (24.7 mm SD ±1.76). That said, other population-based studies also cite averages more consistent with our findings (24 ± 1.57[13]).

These data may reflect an increasing prevalence of myopia in the community, for which there is an emerging body of evidence for, particularly in the Australasia region.[14,15] Alternatively, our study results may also represent a higher-risk demographic of patients referred to the surgeon at hand, as our findings were based on a single surgeon cohort.

The main limitation of this study is the non-random sample of more severely affected FECD eyes, as selection was based on FECD patients who required corneal transplant. Given this bias, there is a possibility that the results reflect a potential tendency of FECD patients with shorter eyes to require surgery more often than other FECD patients. Pitts and Jay[4] suggest this is not the case. They found no significant difference in AL ($p > 0.05$) or ACD ($0.05 < p < 1$) between advanced FECD with corneal edema or previous surgery and those without edema, suggesting that both early and advanced FECD patients can be regarded as a uniform population. Nonetheless, a truly random sample of FECD patients remains ideal and would be recommended for further research.

The strengths of the study include the large sample size of the FECD cohort (particularly compared with previous studies on FECD patients) and use of average measurements from both eyes for each subject. This approach, as opposed to using data from each eye separately to boost sample size, has been shown to reduce the risk of type 1 error.[16]

Our findings make a valuable contribution to the existing evidence, particularly in the profiling of FECD patients, with biometric data that has not yet been published in the literature. Given the continual advances in surgical outcomes of lamellar transplant, a close focus on prognostic factors and surgical considerations remains imperative.

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Anterior segment optical coherence tomography of intrastromal corneal cysts

Deepmala Mazumdar, Barsha Lal, Rashima Asokan
Medical and Vision Research Foundation, Sankara Nethralaya, Chennai, India; Elite School of Optometry, Chennai, India

Abstract
We report a case of six-year-old boy who presented with a progressive intracorneal cyst in the left eye. Anterior segment optical coherence tomography (AS-OCT) was performed, and it showed the location of the cyst in the corneal stroma. Its dimension was measured to be 7.09 × 2.12 mm. The cyst aspiration was successfully done. AS-OCT helped in the management and follow-up of the condition.

Keywords: *anterior segment, AS-OCT, intracorneal cyst*

Introduction

Intracorneal cysts are uncommon, progressive lesions.[1,2] The intracorneal cysts reported so far include epithelial cysts, intrastromal cysts, and pseudocysts.[3,4] In most of the cases, intracorneal cysts were found secondary to trauma or surgery such as cataract extraction, keratoplasty, or any other surgical intervention of cornea.[4,5] In congenital cases, the origin is not known.[5] It would also be misdiagnosed as foreign bodies, herpetic keratitis, and sclerosing keratitis.[3,5,6] These cysts are often found to be progressive in nature, which can cause deterioration of vision by involving the visual axis and can result in cosmetic deformity.[3,6]

Anterior segment optical coherence tomography (AS-OCT, Visante OCT; Carl Zeiss Meditec AG, Jena, Germany) is a noninvasive imaging technology, performed in sitting position, and provides detailed cross-sectional imaging of ocular anterior segment structures. AS-OCT uses infrared light, and imaging is based on the principle of low-coherence interferometry. It measures the delay of infrared light reflected from tissue structures.[7,8] AS-OCT is found as a valuable tool in diagnosing and monitoring the treatment progress in cases like ocular trauma and tumors.[7,8]

Here, we report a case of six-year-old boy with a progressive intrastromal corneal cyst followed up with AS-OCT.

Correspondence: Ms. Rashima Asokan, Medical and Vision Research Foundation, Sankara Nethralaya, Chennai, India.
E-mail: rashi.ashok@gmail.com; rashima@snmail.org

Case report

A healthy six-year-old boy presented to the clinic with slowly progressing white opacity on cornea associated with mild pain, photophobia, and watering in the left eye since birth. He was complaining of diminution of vision in the left eye. There was no trauma, surgery, or any other significant medical history. His birth history was found normal. There was no significant family history reported. He reported that he was diagnosed to have the corneal cyst in his left eye elsewhere and underwent drainage with transscleral cryotherapy (TSC) with fibrin glue four years ago. His visual acuity for distance was found to be 6/6 in the right eye and 2/60 in the left eye. Slit lamp examination revealed whitish corneal opacity in the left eye covering the pupillary area sparing 0.5 mm superotemporally; the iris was not adherent (Fig. 1).

AS-OCT was done in four quadrants to locate the cyst exactly and its extension. The cyst was located in corneal stroma extending 360°, and the dimension was measured as 7.09 × 2.12 mm (Fig. 2). Central corneal thickness was found as 2,000 µm.

As the cyst was found sight-threatening, it was aspirated with trichloroacetic acid. The surgery was uneventful. Follow-up on the first day after surgery showed collapsed cyst cavity and mild corneal edema with a small corneal epithelial defect. The patient was comfortable and no specific complaint was reported. The patient returned to the clinic nine months after surgery.

Examination revealed his best corrected visual acuity of 6/6 for the right eye and 6/36 for the left eye. Postoperative slit lamp examination revealed the presence of mild scar in the left eye. AS-OCT was repeated to check if the cyst was

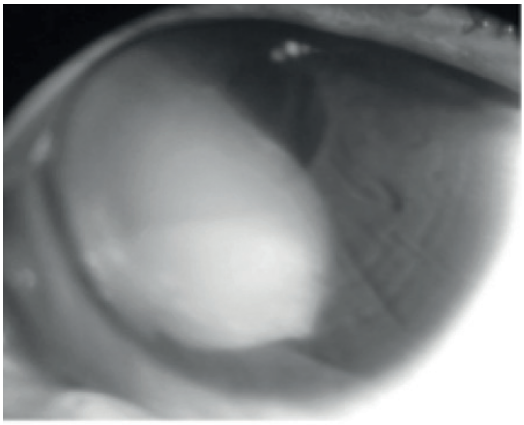

Fig. 1. Preoperative silt lamp image of cyst.

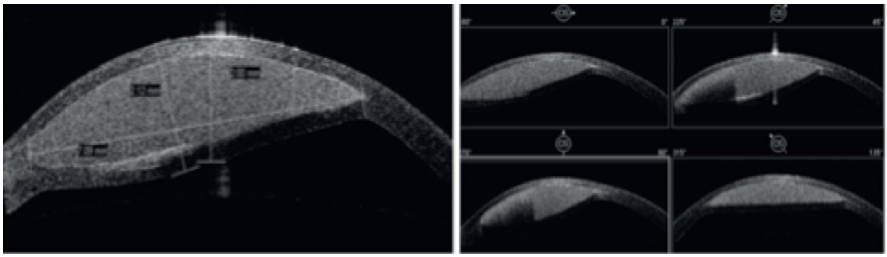

Fig. 2. Preoperative AS-OCT image with dimensions and extension of cyst.

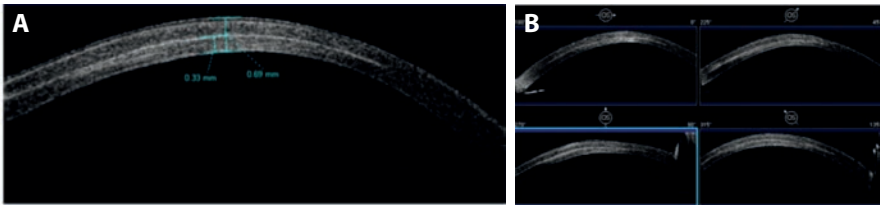

Fig. 3. (A) Postoperative AS-OCT high-resolution corneal image showing central corneal thickness and scar depth. (B) Postoperative AS-OCT corneal quadrant image.

present, and the cyst was found to be completely resolved (Fig. 3A and B). Scar was measured to be 330 µm, and the central corneal thickness was reduced to 690 µm (Fig. 3A).

Patient's left eye vision was not improving even after cyst aspiration, and he was diagnosed as amblyopic in the left eye and was advised for part-time occlusion therapy in the right eye for four hours in a day in order to regain his vision.

Discussion

Cyst progression is indolent in nature and generally painless.[6,9] Thus, surgical excisions are not advised until there is a threat to vision by the cyst or it is progressive.[9] There are different treatment modalities reported in the literature. It includes cyst aspiration, drainage, cyst wall excision, cryotherapy, and lamellar or penetrating keratoplasty.[6,9]

To date, slit lamp photography has been used to detect progression and follow-up of cases with intracorneal cysts, which does not provide the actual information regarding the extension of the cysts and is not reproducible.

AS-OCT allows precise diagnosis of these cysts by providing exact location and even permits to measure the dimension of the cyst. Preoperative AS-OCT findings enabled the surgical decision by providing dimension quantitatively, and postoperative following up on the case becomes easier. In AS-OCT, cornea can be imaged in four quadrants together and it enables 360° scanning.

Therefore, the extension of the cysts can be imaged. Differential pachymetry map can be generated automatically and is helpful in following up the case. Unlike ultrasound biomicroscopy, AS-OCT does not require direct probe contact to the eye.

Conclusion

AS-OCT is easy to perform and is not time-consuming. This will help in monitoring the progression of cysts with quantitative measurements. This case report highlights the use of AS-OCT in the management of intrastromal corneal cysts.

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SITA standard testing with Humphrey visual field analyzer versus full threshold testing with frequency doubling perimetry: a comparison of patient preference and perception

Najiya Sundus Kadavath Meethal[1], Velumuri Lokapavani[1], Rashima Asokan[1,2], Lingam Vijaya[1], Ronnie George[1]

[1]Glaucoma Services, Medical Research Foundation, Sankara Nethralaya, Chennai, India; [2]Elite School of Optometry, Chennai, India

Abstract

Purpose: *To compare patient preference for Swedish Interactive Threshold Algorithm (SITA) standard 24-2 protocol in Humphrey visual field analyzer (HVF) and full threshold N-30 protocol in frequency doubling perimetry (FDP) by primarily evaluating their perception about the test procedure and test targets along with surveying the factors that influence the patient concentration during perimetry and elements that determine the level of perimetry task difficulty.*

Methods: *This study enrolled a subset of subjects from the Chennai Glaucoma Study. Each subject underwent a comprehensive ophthalmic examination after which they were randomly allocated to perform HVF and FDP with a 30-minute interval between the two procedures. SITA standard 24-2 protocol in HVF and full threshold N-30 protocol in FDP were used. This was followed by the administration of a questionnaire that mainly assessed the components such as (a) the patient preference for test procedure and test targets, (b) the factors influencing the patient concentration during perimetry performance, and (c) the impression about the level of perimetry task difficulty. The patient responses from the survey for each of the subcategories were obtained and analyzed using Chi-square test.*

Results: *A total of 42 subjects with a mean age of 59.7 (SD 9.7) years were included, among which 18 (42.86%) were male and 24 (57.14%) were female. Thirty-two (76.19%) subjects felt both FDP and HVF were easy to perform, eight subjects (19.05%) felt that both perimetry techniques were difficult to perform, and two subjects (4.76%) found FDP procedure was easier than HVF, whereas the distribution was not statistically significant (Chi-square, $p = 0.7$). Pressing the button as a response to peripheral stimulus perception and inability to maintain steady central fixation for prolonged duration were the most commonly reported factors that influenced the level of difficulty of the perimetry tasks. A dark room ambience set for performing HVF was preferred by 32 (76.20%) subjects.*

Correspondence: Dr Ronnie George, Director-Research, Senior Consultant Glaucoma Services, Medical and Vision Research Foundation, Sankara Nethralaya, 18, College Road, Chennai 600 006, India.
E-mail: cgscedis@gmail.com

Conclusion: *There was no significant difference in the patient preference for test procedure and peripheral test targets. A black central fixation as in FDP and dark room ambience set for HVF were preferred.*

Keywords: *frequency doubling perimetry, full threshold perimetry, Humphrey visual field, patient preference*

Introduction

Standard automated perimetry (SAP) and frequency doubling perimetry (FDP) are two alternate technologies available to quantify the extent and degree of visual field loss due to glaucoma.[1] The Humphrey visual field analyzer (HVF) with SAP (750 I series; Carl Zeiss Meditec, Dublin, CA, USA) estimates differential light sensitivity using white targets and is considered as the gold standard in evaluating the visual field.[1,2] The frequency doubling perimetry (FDP) (Welch Allyn, Skaneateles Falls, NY, USA, and Carl Zeiss Meditec, Dublin, CA, USA) utilizes low-spatial-frequency sinusoidal grating target. It is a rapid, compact, and effective method of assessing the visual field, thus used as a screening tool.[3,4] The two techniques differ in various aspects such as the test strategy (type of central fixation and peripheral targets), test protocol, test duration, seating posture, type of eye patching, illumination of testing environment, and also in learning curve.[5,6]

Previous studies have reported a strong correlation between FDP and SAP while predicting visual field deficits with good concordance with respect to sensitivity and specificity.[5,6] Since perimetry is a psychophysical procedure that relies on precise subjective responses for determining sensitivity threshold, evaluating patient preference to either of these techniques might have clinical significance. Assessment of patient preference with respect to testing method, target characteristics, physical and mental aspects affecting the test performance, the levels of difficulty of the perimetry tasks, and so on, can help investigators to develop future prototypes of perimeters.

Therefore, this study aimed at comparing patient preference for Swedish Interactive Threshold Algorithm (SITA) standard 24-2 protocol in HVF and FDP by primarily evaluating their perception about the test procedure and test targets along with surveying the factors that influence the patient concentration during perimetry and elements that determine the level of perimetry task difficulty.

Materials and methods

Study population

This study included a cohort of subjects from the urban division of the Chennai Glaucoma Study (CGS), which was a population-based cross-sectional study. The design and methods of CGS were published earlier.[7] The study was approved by the Institutional Review Board, Vision Research Foundation, Chennai, and a

written informed consent was obtained from all subjects. All the study participants underwent a comprehensive ophthalmic examination including objective and subjective refraction, anterior segment examination using slit lamp biomicroscopy, Goldmann applanation tonometry, grading of the lens opacification based on lens opacification classification system II (LOCS II),[8] and visual field assessment using HVF and FDP followed by dilated fundus examination. The right eye of subjects with visual acuity better than 0.2 log MAR with cataract less than NII, CI, and PI on LOCS II were included. Subjects with any corneal or retinal pathology that would affect perimetry performance or test reliability were excluded.

Each subject was randomly allocated to perform HVF and FDP, and the order of perimetry was determined by simple randomization approach by flipping a coin. A minimum of 30 minutes of interval/rest was provided between the two procedures. Examiner gave verbal instructions in the subject's vernacular language or in English before and during the course of testing. All subjects had an experience of performing either of these perimetry techniques more than once in the past. In both the perimetry techniques, performance with fixation losses of >20%, false negatives, and false positives of >33% were considered unreliable, and the test was repeated in such responses.[9] The test was also repeated in cases with artifacts and with field defects that were not corresponding to structural abnormality of the optic nerve head.

Components of questionnaire

The questionnaire was administered orally to all subjects. The questionnaire was framed in English and was administered by the interviewer in the local language (Tamil). The translation was validated before its incorporation in this study. The questionnaire had a total of 13 questions (Appendix A), which were generally pertaining to three categories such as (a) the patient preference for test procedures and test targets, (b) the factors influencing the patient concentration during perimetry performance, and (c) the impression about the level of perimetry task difficulty.

Questions formulated for assessing the patient preference included the easiness/comfort of perimetry procedures, preference for central fixation, and peripheral test targets used in both the perimetry techniques in terms of recognition. Questions regarding physical factors such as noise distractions during the course of testing, type of eye patching used, and mental factors like fear for failing/repeating the test, fatigue, and so on, were included in the questionnaire, which was thought to have potential influence on the patient's concentration while performing the test.

The impression about the level of perimetry task difficulty was analyzed by incorporating questions related to difficulty in maintaining steady central fixation for a prolonged duration, difficulty in recognizing peripheral targets

against the used background intensity, and difficulty in pressing the response button during peripheral stimulus perception.

Questions for understanding the preferred time gap between the tests as well as the perception about the ambience of the testing environment were integrated. The obtained patient responses were coded, which were used along with the responses obtained using Likert scales for performing Rasch analysis.[10]

The patient responses obtained from the survey for each of the subcategories were analyzed using Chi-square test. The McNemar's test was conducted for comparative analysis of responses obtained from those questions that were based on Likert scale method. The five-point Likert scale was converted into a dichotomous scale for the McNemar's probability value. For those questions where 2 × 2 tables could not be formed without empty cells, Fisher's exact test was performed.

Results

Among 42 subjects, 18 (42.86%) were male and 24 (57.14%) were female and the mean age of the group was 59.7 (SD 9.7) years. Sixteen subjects were diagnosed to have angle-closure glaucoma, 11 had open-angle glaucoma, 14 had ocular hypertension, and 1 subject was normal. The order of testing was randomized and 31 subjects (73.81%) performed visual field testing by FDP prior to HVF, whereas 11 subjects (26.19%) performed HVF first. Twenty subjects (47.62%) had performed the test four times on both the machines, 18 subjects (42.86%) have undergone the test three times, and 4 subjects (9.52%) underwent the test twice prior to inclusion to the study.

Thirty-two subjects (76.19%) showed equal preference to the test procedures in terms of easiness and comfort level whereas 8 subjects (19.05%) felt difficulty in performing both the procedures and 2 subjects (4.76%) found FDP was easier than HVF, and the difference was not statistically significant ($p = 0.79$, 95% confidence interval: −0.127 to 0.223). Thirty subjects (71.43%) preferred a central black fixation target as in FDP and 17 subjects (40.47%) preferred a central yellow fixation target of HVF, 11 subjects (%) were comfortable with either of the fixation target (Chi-square, $p = 0.008$). Twenty-eight subjects (66.67%) had difficulty in responding to target stimuli on both the perimetry techniques and the other 14 subjects (33.34%) had no difficulty with either of the target stimuli. Eleven subjects (26.19%) found both of the testing procedures to be equally fast, 24 subjects (57.14%) found FDP to be faster, 6 subjects (14.29%) felt HVF was comparatively fast ($p = 0.0001$), and 1 subject felt neither of the perimetry techniques was fast.

Time taken to perform both perimetry procedures was analyzed. Mean

test duration of HVF was found to be 342.94 (SD 58.60) seconds, whereas the mean test duration for FDP was 325.40 (SD 18.96) seconds, and there was no statistically significant difference in test duration between the two perimetric techniques (p = 0.062, 95% confidence interval: −1.002 to 38.191).

When analyzing the mental factors that can influence patient concentration during test performance, 26 subjects (61.90%) were responded to have fear of failing the test and 27 subjects (64.29%) had fear of repeating the entire perimetry procedure. In 16 subjects (38.10%), the test was repeated, of which 9 subjects (56.25%) were asked to repeat the test once and 7 (43.75%) subjects repeated the test twice. When subjects were asked to recollect the number of times the test was repeated, three subjects were unable to recall the number of times they repeated the perimetry procedure. Physical factors such as noise distractions during the test procedure and type of patch used for the nontested eye (p = 0.614) were not reported as significant factors affecting their concentration.

The responses obtained for those questions included for analyzing the impression about the level of perimetry task difficulty are summarized in Table 1.

A dim lit testing environment as in HVF was preferred by 32 subjects (76.19%) and 14 (43.75%) of these did not prefer the illuminated testing environment in case of FDP (p = 0.04). The mean preferred gap by the patients between both the procedures was 15.91 (SD 7.35) minutes.

Table 1. Comparative analysis of factors influencing the difficulty level of perimetry tasks

Questions	Easier		p value
	HVF	FDP	
Was the testing procedure easy/difficult?	32	34	0.79
Was the maintenance of steady central fixation easy/difficult?	17	30	0.008
Was the recognition of peripheral test targets easy/difficult?	8	8	NA
Was pressing the response button easy/difficult?	14	14	NA

NA: not applicable

Discussion

The assessment of visual function using perimetry technique is an essential component in glaucoma diagnosis and SAP is considered as the reference standard for plotting the visual field. SITA standard 24-2 protocol in HVF evaluates visual sensitivity at 54 test locations within the central 24° visual field. This protocol relies on summary indices and Glaucoma Hemifield Test for detecting glaucomatous field loss. In comparison with this gold standard, FDP is an effective screening mode in clinical setting with a sensitivity of 78.1 and 89.1% specificity.[11] FDP is recommended as a promising method for identifying retinal ganglion cell damage at an early stage compared with the SAP and effective in monitoring visual field progression.[12,13]

Diagnostic and screening tests should be sensitive, specific, and patient acceptable. The patients had equal preference for overall comfort with both the procedures and a black central fixation target as in FDP was highly preferred compared with yellow target as in HVF, in which the target contrast against the testing background could be considered as a possible influential factor. No test preference for either of the peripheral test stimuli was found. Although results show that FDP is faster than HVF by 18 seconds, there was no statistically significant difference ($p = 0.062$).

Fear of failing/repeating the test was found as the most commonly reported psychological factor that might have potential influence on patient's concentration that can affect the reliability of test measurements. Any kind of noise distractions from conversations or any other source either within the test room/outside did not have a significant effect on the patient concentration. Barkara *et al.* had described that conversing on cellular phones with the use of hands-free headsets caused some subjects to miss significantly higher number of points, react slower to each stimulus, and perform the test with less precision, and moreover, there was a significant increase noted in fixation loss and test duration.[14]

Pressing the button as a response to peripheral stimulus perception and inability to maintain steady central fixation for prolonged duration were the most commonly reported factors that increased the level of difficulty of the perimetry tasks. A darker room ambience of HVF was more preferred than illuminated testing room in case of FDP. Dark rooms were preferred due to factors like ease of perceiving target in a darker environment compared with normal room illumination.

To analyze if the patients were given enough time gap in between the two tests, the patients were asked to quote their preferred rest duration (in minutes). All the patients mentioned preferred time gap of 15.91 ± 7.35 minutes, which was significantly less than the provided time interval. Therefore, the provided

time gap was considered to be sufficient for overcoming the fatigueness that arise from performing the perimetry. This will be relevant information that can be considered during the administration of two perimetry procedures consecutively.

One of the limitations of this study was that all the participants had previous experience with both the perimetric procedures since they belonged to CGS[7] follow-up study, which would have led to a patient bias toward either of these testing procedures. Even if the order of performing the perimetry procedures were randomly decided using simple randomization technique, a large proportion (73.81%) of patients underwent FDP prior to HVF. Unequal participants among the two groups would have been probably due to the smaller sample size which might have a potential bias on the patient's perception.[15] A sufficient time gap was provided between the two procedures with a thought to minimize the effect of fatigueness. Considering block randomization would have been a better way to ensure a balance in sample across the two groups over time. It was ideal to consider few external factors such as waiting time and comfort level in waiting room for an elaborate view of potential elements that influence patient preference and perception about perimetry testing.

Conclusion

There was no significant difference in the patient preference for test procedure and peripheral test targets while performing visual field evaluation using HVF and FDP. A black central fixation as in FDP and dark room ambience set for HVF were preferred. The central black fixation target as in FDP and a dark room ambience as in HVF were mostly preferred by the study participants.

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Appendix A

Questionnaire to compare patient's comfort in taking the visual field test using the HVF and the FDP

1. How many times have you taken the eye tests using
   a. HVF
      i. 0
      ii. 1
      iii. 2
      iv. 3
   b. FDP
      i. 0
      ii. 1
      iii. 2
      iv. 3

2. Which of the following do you feel is easier to see while taking the test?
   a. Vertical lines
   b. White spots

3. Do you find it difficult to concentrate on the central fixation point while taking the test?
   a. Yes
   b. No
   c. Unable to decide

4. Which machine are you more comfortable with when you are required to take the test?
   a. HVF
   b. FDP
   c. Neither
   d. Both

5. Which among the two machines do you think is a faster method to take the test?
   a. HVF
   b. FDP
   c. Neither
   d. Both are equal

6. Which among the two machines do you think is an easier method to take the test?
   a. HVF
   b. FDP
   c. Neither
   d. Both are equal

7. Do you get disturbed and hence not perform the test accurately because of any of the following reasons in your immediate environment?
   a. Noise from outside/conversations that take place in the room where the test is conducted

Very high	High	Less	Very less	Not at all

   b. Fear of failing the test

Very high	High	Less	Very less	Not at all

c. Fear of being asked to repeat the test

Very high	High	Less	Very less	Not at all

d. Black/white patches on the other eye

Very high	High	Less	Very less	Not at all

e. Fatigue/lack of enough sleep

Very high	High	Less	Very less	Not at all

If you have filled in option (e):

8. How many hours of work do you put in on an average day?
   a. 4-6 hours
   b. 6-8 hours

9. Do you work overtime/night shift, etc…?
   a. Yes
   b. No

10. Do you prefer to take the test in a
    a. Dark room
    b. Brightly illuminated room

11. How many times were you asked to repeat the test the last time you took it?
    i. 0
    ii. 1
    iii. 2
    iv. Can't recall

12. How long a gap do you require before retaking the test?

    _____

13. Which test did you take first?
    a) FDP
    b) HVF

14. Kindly grade the following test conditions with respect to the difficulty/ comfort level.

Condition	Machine	Very difficult	Moderately difficult	Mildly difficult	Easy	Very easy
Testing procedure	HVF					
	FDP					
Ability to comprehend instructions	HVF					
	FDP					
Pressing the button	HVF					
	FDP					
Being able to focus on the fixation point	HVF					
	FDP					
Ability to see the targets against the background	HVF					
	FDP					

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Benzalkonium chloride corneal toxicity post-cataract surgery

Keith Ong[1,2,3,4], Leonard Ong[4,5,6]

[1]Department of Ophthalmology, Northern Clinical School, University of Sydney, Sydney, Australia; [2]Department of Ophthalmology, Royal North Shore Hospital, Sydney, Australia; [3]Department of Ophthalmology, Sydney Adventist Hospital, Sydney, Australia; [4]Department of Ophthalmology, Chatswood Private Hospital, Sydney Australia; [5]Ophthalmology Clinic, Macquarie University Hospital, Sydney, Australia; [6]Department of Clinical Medicine, Faculty of Medicine and Health Sciences, Macquarie University, Sydney, Australia

Abstract

Two patients with presumed benzalkonium chloride (BAK) corneal toxicity after routine cataract surgery are presented. Patient 1 had corneal stroma and Descemet's membrane folds. Patient 2 had moderate superficial punctate epithelial erosions (SPEE). They were on Chlorsig, Maxidex, and Acular eye drops tds postoperatively. The corneas of these two patients improved when BAK was removed or minimized from the postoperative eye drop regimen. Two vials of 1 ml dexamethasone 4mg/ml for injection were added to Chlorsig 10 ml bottle to substitute for Maxidex eye drops.

BAK toxicity should be suspected when the cornea is not as clear as expected postoperatively. A practical way to eliminate BAK from postoperative eye drops is described, and would be useful until pharmaceuticals mass-produce BAK-free steroid eye drops economically.

Keywords*: benzalkonium chloride (BAK), cataract surgery, corneal toxicity*

Case Report

Patient 1

A 69-year-old male underwent routine left cataract phacoemulsification and posterior chamber intraocular lens (PCIOL) (Alcon SN60WF). Preoperative endothelial cell count (ECC) was 2880/mm^2 and central corneal thickness (CCT) was 568 microns. Visual acuity (VA) with myopic correction was 6/9 on day 1 postoperative. At 1 week postoperative, (VA) was 6/18, with corneal stroma and Descemet's membrane folds, minimal superficial punctate epithelial erosions (SPEE) fluorescein staining (Fig. 1 and Fig. 2), ECC of 2524/mm^2, and CCT of 665 microns. There were occasional cells in the anterior chamber and no conjunctival

Correspondence: Dr. Keith Ong, 2 Railway Avenue, Eastwood NSW 2122, Sydney, Australia.
E-mail: keithong@optusnet.com.au

inflammation. Intraocular pressure (IOP) was 14 mmHg bilaterally. He was on a postoperative regimen of Chlorsig (chloramphenicol 0.5%, Aspen), Maxidex (dexamethasone 0.1%, Alcon), and Acular (ketorolac 0.5%, Allergan) drops tds. BAK corneal toxicity was suspected.

Two vials of 1 ml Dexamethasone 4mg/ml for injection were added to a Chlorsig 10 ml bottle, and Acular tds was replaced with Ilevro (nepafenac, Alcon) once daily. At 2.5 weeks, there was no significant improvement in corneal appearance. As Ilevro contained BAK, Ilvero was stopped and replaced with Indomethacin 25 mg daily orally. He continued with Chlorsig-Dexamethasone tds. At 6 weeks, he mentioned that he had noticed improvement after a week on the new regimen, and VA was 6/9 with much improvement of corneal stroma and Descemet's membrane folds, ECC of 2882/mm^2, and CCT of 594 microns.

When he underwent right cataract phacoemulsification and PCIOL, he was prescribed Chlorsig-Dexamethasone tds and Indomethacin 25 mg orally daily. There was no corneal problem. VA was 6/9 on day one and at one month.

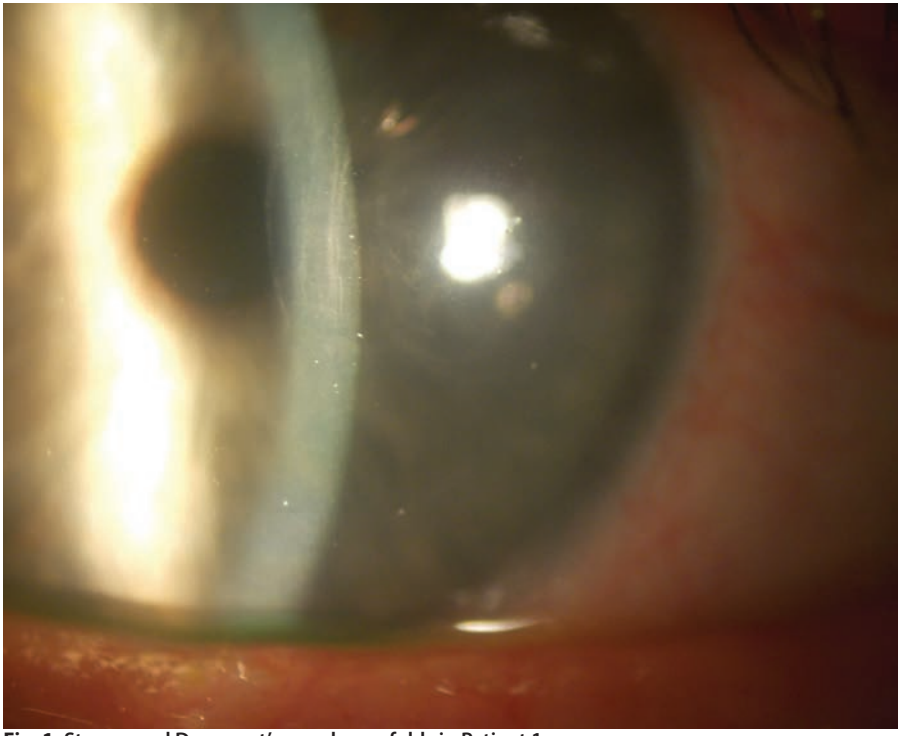

Fig. 1. Stroma and Descemet's membrane folds in Patient 1.

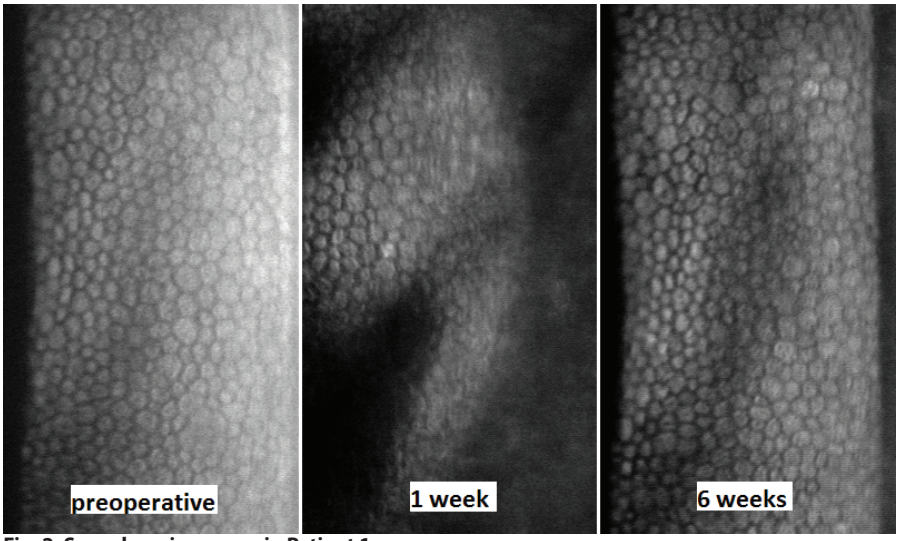

Fig. 2. Specular microscopy in Patient 1.

Patient 2

A 65-year-old female underwent routine right cataract phacoemulsification and PCIOL (Alcon SN 60WF). She has a past history of dry eye controlled with tear supplements. On day 1 postoperative, VA was 6/9 with myopic correction. At 1-week postoperative, VA was 6/12 corrected and IOP was 16 mmHg bilaterally. She had extensive SPEE fluorescein staining of the cornea, with no significant corneal stroma or Descemet's folds (Fig. 3). She was on Chlorsig, Maxidex, and Acular drops tds. She was changed to Chlorsig-Dexamethasone tds and Acular once daily. At 5 weeks, SPEE improved and VA was 6/9 with myopic correction. When she underwent left cataract phacoemulsification and PCIOL, she was on Chlorsig-Dexamethasone tds and Acular once daily. There was no corneal problem and VA was 6/9 on day one and at one month postoperative.

Discussion

BAK toxicity usually presents as corneal SPEE.[1,2] Corneal edema[3] with corneal stroma and Descemet's folds is uncommon. Mechanisms proposed include damage to corneal epithelial cells by disruption of cell tight junctions and toxicity to the corneal endothelium.[1,2,4] BAK causing mitochondrial dysfunction may play a part in the corneal changes.[5]

Maxidex and Acular contain BAK, and when BAK is instilled six times a day, corneal toxicity is more likely to occur in a shorter time frame. Chlorsig contains polymercuric acetate as preservative. When BAK was eliminated or reduced from

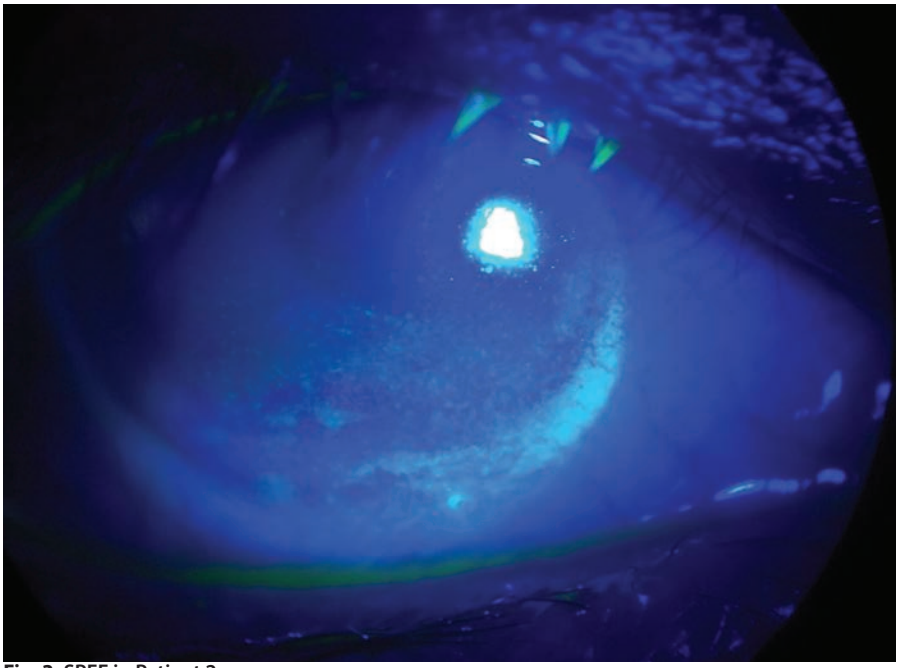

Fig. 3. SPEE in Patient 2.

the eye drop regimen, the cornea of these two patients did not have any significant corneal stroma, Descemet's folds, or SPEE.

BAK allergy is less common, and the conjunctiva and eyelid skin are inflamed and itchy. Maxidex eye drops contain BAK, and when used, the dexamethasone steroid often masks the conjunctival inflammation, whereby only the eyelid and lid margin develop inflammation and redness.

Hence, BAK toxicity should be suspected when the cornea is not as clear as expected postoperatively. A practical way to eliminate BAK from postoperative eye drops is described, and would be useful until BAK-free steroid eye drops are easily available and affordable.

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Prophylactic corneal cross-linking in LASIK surgery: effects on visual outcome and recovery time

Dominique Clare Oh[1], Yiong Huak Chan[2], Sao Bing Lee[3], Jovina Li Shuen See[3]

[1]Raffles Institution, Singapore, Singapore; [2]Biostatistics Unit, Yong Loo Lin School of Medicine, Singapore, Singapore; [3]Shinagawa Eye Centre, Singapore, Singapore

Abstract

Introduction: *Collagen cross-linking is a useful adjunct in preventing corneal ectasia after laser-assisted in situ keratomileusis (LASIK). This study aimed to evaluate whether prophylactic cross-linking in IntraLase LASIK affects optimum visual outcome and recovery time in the immediate post-surgery period and is associated with any side effects.*

Methods: *This was a retrospective case study on the right eyes of 100 Chinese subjects aged 18 to 40 years who underwent IntraLase LASIK. Fifty subjects who underwent cross-linking after completing LASIK (Group A) were compared with 50 subjects who did not undergo LASIK (Group B). Cases were evaluated for pre- and post-operative spherical equivalent, uncorrected distance visual acuity (UDVA) and corrected distance visual acuity (CDVA), recovery time and presence of side effects.*

Results: *At 1 week post-LASIK, mean (SD) UDVA of Group A subjects was poorer than Group B, at 1.05 (0.19) vs 1.17 (0.19) ($p = 0.036$); however, there was no significant difference in CDVA ($p = 0.095$). By 1 month post-LASIK, differences in both UDVA and CDVA were insignificant ($p = 0.055$, 0.106, respectively). Mean recovery time was 2.72 (95% confidence interval [CI] = 0.64-4.7) days longer in Group A ($p = 0.010$), although by 1 month post-LASIK, both groups were able to achieve CDVA equal to or better than that achieved pre-LASIK. Incidence of mild inflammation and dry eyes post-LASIK was similar in both groups ($p = 1.00$, 0.749, respectively); no other complications were observed.*

Conclusion: *No differences in visual outcomes at and occurrence of side effects at 1 month post-LASIK were observed between subjects who underwent cross-linking prior to refractive surgery and those who did not. However, the group that underwent cross-linking had a slightly longer mean recovery time. Our study supports prophylactic cross-linking as a safe procedure that does not affect immediate visual outcomes among the Chinese population when used in adjunct with LASIK surgery.*

Keywords: *collagen cross-linking, corneal ectasia, corneal refractive surgery, LASIK*

Correspondence: Dominique Clare Oh
E-mail: niqueclareoh@yahoo.com.sg

Introduction

Corneal ectasia is a serious complication that can arise after corneal refractive surgery as a result of corneal weakening due to thinning of the corneal stroma.[1] Patients who develop corneal ectasia may experience increased myopia and/or astigmatism, associated with a loss of uncorrected and sometimes even best-corrected visual acuity.[2,3] This is accompanied by characteristic keratometric steepening, in particular an asymmetric inferior corneal steepening, that is evident following corneal refractive surgery.[3] Significant risk factors for corneal ectasia include the presence of forme fruste keratoconus pre-operatively, a high degree of myopia or astigmatism correction performed during corneal refractive surgery, and low residual stromal bed thickness of the cornea post-operatively.[4] The incidence of corneal ectasia has been reported to range from 0.04% to 0.66%.[1,4-6]

Corneal collagen cross-linking has been performed for close to two decades since 1998 in patients with established corneal ectasia, such as in keratoconus patients. The technique originally involved the application of riboflavin and use of a photosensitizer, with exposure to ultraviolet (UV) light for 2 hours in order to form new chemical bonds between adjacent collagen fibrils in the cornea.[7-10] Cross-linking in these patients has been widely reported to have a success rate of 70% in arresting corneal ectasia or, in some cases, even resulting in a 65% improvement of best-corrected visual acuity.[10]

In recent years, with the development of the Avedro cross-linking system, the necessary exposure time to UV light has been significantly shortened to just 1 to 10 minutes. This accelerated cross-linking procedure has been suggested to be safe and effective in halting post-operative laser-assisted in situ keratomileusis (LASIK) ectasia progression over a 1- to 2-year follow-up period, with patients achieving gains in refractive and keratometric stability, as well as uncorrected distance visual acuity (UDVA) and corrected distance visual acuity (CDVA).[11-13] Thus, the use of corneal collagen cross-linking as a prophylactic corneal strengthening procedure in patients undergoing refractive surgery who are at higher risk of developing corneal ectasia has now been made possible.

Although the efficacy of the procedure may be inferred from aforementioned studies where cross-linking was performed in keratoconus patients,[10] as well as in studies where less regression was observed in LASIK patients who underwent the procedure,[11-13] it remains difficult to confirm actual efficacy in preventing corneal ectasia where cross-linking is performed as a prophylactic measure in patients undergoing elective corneal refractive surgery. In addition, it has been suggested that possible side effects of adjunctive corneal collagen cross-linking could include higher infection rates in the immediate post-operative period due to longer surgical exposure time and an increased risk of corneal scarring,

infiltrates and diffuse lamellar keratitis, which may in turn affect the optimum visual outcomes of LASIK surgery or result in a longer recovery duration. Hence, we chose to evaluate the safety of the procedure in terms of immediate optimum visual outcomes and the time taken to achieve this outcome, as well as associated side effects during the immediate post-operative period. We believe looking at immediate optimum visual outcomes and length of recovery time are important not only in aiding patients to decide on whether to undergo this prophylactic adjunctive procedure but also to help refractive surgeons to provide better pre-operative counselling when advising patients on the procedure.

In our study, we looked at cross-linking using the Avedro system performed prophylactically in a Chinese population undergoing elective IntraLase LASIK surgery.

Methods

A total of 179 patients underwent IntraLase LASIK with cross-linking at the Shinagawa Eye Centre and a total of 601 patients underwent IntraLase LASIK without cross-linking between 1 July 2013 and 1 July 2014. From each of these two groups, an online random number generator was used to select 50 subjects. All subjects were Chinese, aged 18 to 40 years and treated by a single refractive surgeon. Subjects had undergone elective IntraLase LASIK using the iFS IntraLase femtosecond laser and the Schwind AMARIS 750 excimer laser machine. Corneal collagen cross-linking for the 50 subjects in Group A had been performed immediately after completion of IntraLase LASIK using VibeX Xtra (Riboflavin phosphate 2.80 mg/ml). For IntraLase flap thickness of 120 μm, VibeX Xtra was applied to the corneal stroma for 65 seconds and after flap replacement, was activated by UV light for 66 seconds at 30 mW/cm^2, with a total energy of 2.0 J/cm^2.

In this retrospective study, the 50 subjects who had undergone Avedro cross-linking (Group A) were compared to the 50 subjects who had not undergone Avedro cross-linking (Group B). Case records were used to retrospectively evaluate the right eyes of all subjects in terms of visual outcomes, recovery duration and presence of side effects.

For all subjects, post-operative examinations were conducted at 1 day, 1 week and 1 month after LASIK surgery. The post-operative evaluation included UDVA and CDVA assessment using Snellen chart and clinical evaluation using slit-lamp examination for the presence of dry eye using tear breakup test and complications such as epithelial ingrowth and diffuse lamellar keratitis. Patients were also routinely asked whether they experienced any dry eye symptoms and were routinely treated with a tapering course of topical steroid (PredForte) and antibiotic (Cravit) eye drops in the first post-operative week. Subjects who were found to have diffuse lamellar keratitis on the first post-operative day were treated with

additional topical Maxidex eye ointment at night in the first post-operative week.

Main outcomes evaluated were pre- and post-LASIK UDVA and CDVA, pre- and post-LASIK refraction and recovery time (defined as time taken to return to CDVA achieved pre-LASIK). A secondary outcome that was also evaluated was the presence of side effects such as post-operative diffuse lamellar keratitis, dry eyes, epithelial cell ingrowth, infection and other complications.

All analyses were performed using SPSS 24.0 with statistical significance set at $p < 0.05$. Descriptive statistics for numerical variables were presented as mean (SD) and *n* (%) for categorical variables. Differences in post-operative numerical outcomes between the two groups were compared using two sample *T*-test when normality and homogeneity assumptions are satisfied, otherwise Mann–Whitney *U* was performed; Fisher's exact test was used for categorical outcomes. Multivariate analyses using linear regression (for numerical outcomes) and logistic regression (for binary outcomes) adjusting for age, gender, pre-operative spherical equivalent and pre-operative CDVA as well as presence of dry eyes or inflammation were performed.

Results

Of the 50 Group A subjects who underwent cross-linking, 27 were female and 23 were male; the mean age (SD) was 28.3 (4.8) years. Pre-operatively, the mean spherical equivalent (SD) of Group A subjects was −6.2 (2.40) diopters (D) (range: −2.0 to −11.0). Of the 50 Group B subjects who did not undergo cross-linking, 25 were female and 25 were male; the mean age (SD) was 30.1 (5.8) years. Pre-operatively, the mean spherical equivalent (SD) was −4.68 (1.78) D (range: −1.5 to −9.3) ($p < 0.001$). There were no significant differences in age ($p = 0.090$) and gender ($p = 0.689$) between the two groups.

At 1 week post-LASIK, visual outcome, measured by mean decimal UDVA, was not as good in Group A as compared to Group B. Mean decimal UDVA (SD) of Group A was 1.05 (0.19), while that of Group B was 1.17 (0.19) (adjusted $p = 0.036$). The percentage achieving decimal UDVA of 1.0 or better was 84.0% and 94.0%, respectively. However, while mean decimal CDVA (SD) was also slightly poorer in Group A at 1.10 (0.17) compared to 1.21 (0.16) in Group B, the difference was not statistically significant (adjusted $p = 0.095$). The percentage achieving decimal CDVA of 1.0 or better was similar at 96.0% and 100.0%, respectively.

Furthermore, by 1 month post-LASIK, no significant difference in visual outcomes of LASIK surgery, in terms of both UDVA and CDVA, was observed. Mean decimal UDVA (SD) of Group A improved to 1.12 (0.18), while that of Group B improved to 1.21 (0.18) (adjusted $p = 0.055$) (see Fig. 1). The percentage achieving decimal UDVA of 1.0 or better was the same in both groups at 94.0%. Mean decimal CDVA of Group A and Group B was 1.17 (0.17) and 1.24 (0.15), respectively (adjusted

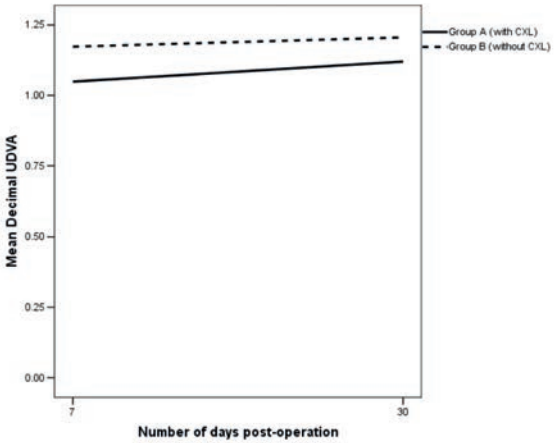

Fig. 1. Mean decimal UDVA from 1 week to 1 month post-LASIK.

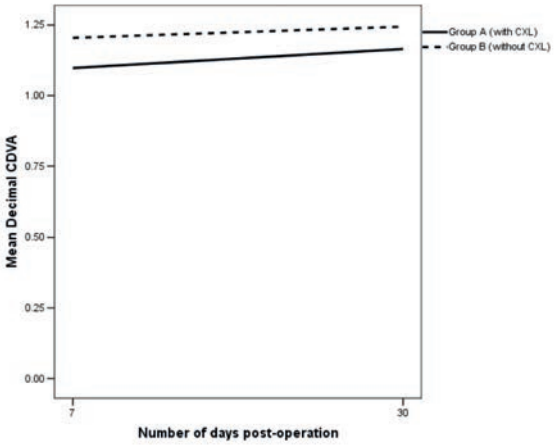

Fig. 2. Mean decimal CDVA from 1 week to 1 month post-LASIK.

p = 0.106) (see Fig. 2), and 100.0% of subjects in both groups achieved decimal CDVA of 1.0 or better. Although mean UDVA and CDVA of Group A subjects remained slightly lower than Group B, differences were not statistically significant.

Mean recovery time (SD), defined as the time taken to return to CDVA achieved pre-LASIK, was longer for Group A subjects at 5.40 (5.9) days (range: 1-30 days) compared to 2.68 (2.7) days (range: 1-7 days) for Group B subjects, adjusted p = 0.010. By 1 month post-LASIK, however, 100.0% of subjects in both groups

were able to achieve decimal CDVA equal to or better than their pre-LASIK CDVA.

A similar percentage of subjects in both groups were found to have mild inflammation at 1 day post-LASIK (10% and 12%, respectively, p = 0.749) and 0.0% of subjects in both groups had inflammation at 1 week and 1 month post-LASIK. In addition, the percentage of subjects experiencing dry eyes post-LASIK was equal in both groups at 20.0%. There were no other complications, such as diffuse lamellar keratitis, infection or epithelial cell ingrowth, in either group.

Discussion

A recent ex vivo study by Kanellopoullos *et al.* demonstrated that cross-linking combined with myopic LASIK provides significant increase in corneal stromal rigidity.[13] In view of this biomechanical advantage, it is desirable to consider cross-linking as an adjunct to refractive surgery to reduce risk of developing corneal ectasia post-operatively. However, for cross-linking to be adopted as a prophylactic measure in refractive surgery, it is important to show that the procedure does not adversely affect visual outcomes and is not associated with any side effects.

Unlike previous studies that focused on evaluating the efficacy of prophylactic cross-linking in LASIK surgery for prevention of regression in visual outcomes due to corneal ectasia, our study looked at the effects of the procedure on the optimum visual outcome of LASIK surgery achieved within the immediate post-operative period, as well as the recovery time taken to achieve this outcome. Thus, instead of the longer 1- to 2-year follow-up period of other studies, we focused on the immediate 1 month post-surgery since 100.0% of subjects were able to achieve their pre-operative CDVA within this time period. Since cross-linking has already been suggested to be effective in slowing down regression, patients interested in the procedure would further benefit from knowing if it is associated with any adverse effects, such as infection or prolonged recovery time.

Our study found that prophylactic corneal collagen cross-linking in LASIK surgery may slightly increase the length of recovery time by an average 2.72 days and result in slightly poorer UDVA at 1 week post-LASIK. However, CDVA is not affected even at 1 week post-LASIK. Moreover, eventual optimum visual outcomes, in terms of both UDVA and CDVA, are unaffected by addition of the cross-linking procedure, as evident by how the optimum visual outcomes achieved in both groups at 1 month post-LASIK were similar. Combining the cross-linking procedure with LASIK surgery was also found to be safe as it did not increase the risk of any side effects such as diffuse lamellar keratitis, corneal scarring, dry eyes or epithelial cell ingrowth.

As this was a retrospective case study, however, one limitation was that subjects in the two groups differed in terms of their pre-operative refractive error, with

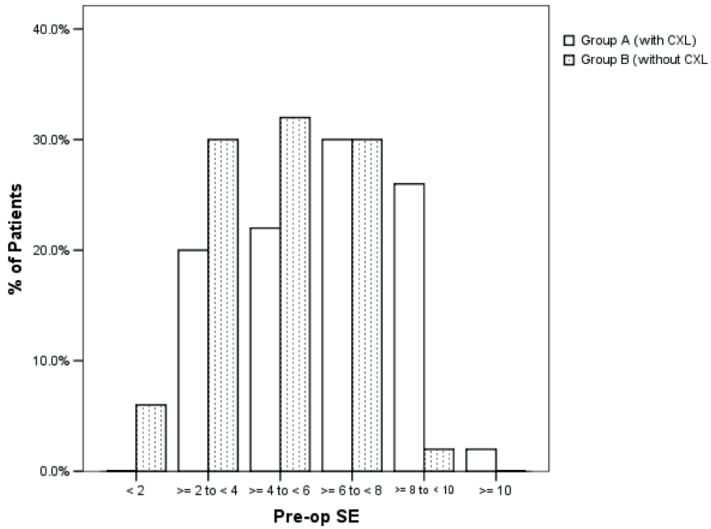

Fig. 3. Distribution of pre-operative spherical equivalent of Group A and Group B subjects.

Group A subjects having significantly higher mean refractive error ($p < 0.001$) (see Fig. 3). The proportion of high myopes was also higher in Group A; 58% had high myopia of −6.00 D and above, compared to 32% of Group B ($p = 0.009$). Since refractive surgery for higher degrees of myopia necessitates a greater amount of ablation depth, which increases risk of corneal ectasia, more high myopes would have opted in for the cross-linking procedure, hence explaining why this group included more high myopes. Therefore, the slightly poorer visual outcome observed at 1 week post-LASIK in Group A may at least be partially attributed to the higher myopia present pre-operatively in these subjects, rather than only to the cross-linking procedure. As such, we tried to correct for these differences in our statistical analysis of results. Another limitation was that presence of side effects of dry eyes was clinically evaluated via the tear breakup test with only fluorescein dye and not using Schirmer's test. Lastly, although all patients managed to return to their pre-operative CDVA and make full recovery within the 1-month timeframe of our study, it could have been interesting to consider an additional follow-up at 3 months.

Conclusion

From our study, although mean recovery time was slightly longer in Group A subjects with cross-linking as compared to Group B subjects without cross-linking at 1 week post-LASIK, eventual visual outcomes at 1 month post-LASIK were

similar. Furthermore, Group A subjects did not experience any additional complications, such as inflammation, dry eyes and epithelial cell ingrowth compared to Group B subjects. Therefore, our results support prophylactic cross-linking as a safe procedure to be used in adjunct with LASIK, with no adverse effects on immediate visual outcome, among the Chinese population.

To further investigate the effects of the cross-linking procedure, a prospective study involving a randomised controlled trial can be considered in future.

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Orbital cellulitis following Caldwell Luc procedure for maxillary sinusitis leading to a rare complication of central retinal artery occlusion

Deepti Mahajan, Gaurav Sharma, Rajeev Tuli
Department of Ophthalmology, Rajendra Prasad Medical College, Kangra, India

Abstract
Posterior orbital cellulitis is a clinical syndrome in which early severe visual loss overshadows or precedes accompanying inflammatory orbital signs. It is an ocular emergency that can threaten life and vision. Central retinal artery occlusion (CRAO) is a very rare condition leading to sudden onset of decreased vision and can even progress to blindness. We report a case of orbital cellulitis following Caldwell Luc surgery in a middle-aged diabetic woman, resulting in the rare complication of CRAO, leading to blindness in her right eye. The development of retinal artery occlusion after orbital cellulitis has not been well documented in literature. A quick diagnosis and close monitoring following sinus surgery is therefore needed to prevent such rare complications to happen.

Keywords: *artery, Caldwell Luc, cellulitis, occlusion, orbital, retina, sinusitis*

Introduction

Central retinal artery occlusion (CRAO) is a very rare condition with an incidence of 1/10,000 of outpatient visits.[1] This event is sudden and devastating, leading to decreased visual acuity.[2] Visual loss following orbital cellulitis can still occur despite prompt diagnosis and management. Acute arterial occlusion is an unusual but known complication of orbital cellulitis.[3] Thus, it is one of the most important conditions in ophthalmology that warrants immediate intervention. We report a rare case of CRAO with posterior orbital cellulitis in a patient operated by Caldwell Luc surgery for maxillary sinusitis.

Case

A 55-year-old diabetic female presented to the ENT outpatient department on 27 March, 2017 with the chief complaint of swelling in the right cheek since 4 days. She was diagnosed with maxillary sinusitis with periorbital cellulitis. On 31 March, 2017, an eye consultation was requested. Visual acuity was 6/12 in the right and

Correspondence: Dr Deepti Mahajan, Senior Resident, Department of Ophthalmology, Rajendra Prasad Medical College, Kangra, Himachal Pradesh, India.
E-mail: mahajandeepti22@gmail.com

left eye. Ocular movements were normal. Fundus examination revealed a normal disc and there were no clinical features suggestive of preseptal or orbital cellulitis. A computed tomography (CT) scan was done, which revealed opacification of the maxillary sinus (right side > left side) with diffuse inflammatory changes in the soft tissue of the right cheek (Fig. 1). Injection ceftriaxone and injection metronidazole was started intravenously. After a complete work up, Caldwell Luc operation was done for pus removal from the maxillary sinus. The patient was given intravenous injections ceftriaxone, metronidazole and paracetamol and tablet levocetirizine. Two days following surgery, the patient reported to the eye department with diminished vision in the right eye. She denied perception of light in the right eye. Fundus examination of the right eye revealed disc pallor, cattle tracking of the vessels in the superior arcade. There was evidence of ischaemic retina (Fig. 2). Left eye fundus examination was normal. Intraocular pressure (IOP) in the right and left eye was 13 mm Hg. A diagnosis of CRAO was made. Ocular massage was done for 5 minutes and investigations were done. Fasting blood sugar was 154 mg, blood profile was normal, ESR was 12 mm/h, electrocardiogram revealed a normal study, carotid Doppler revealed mild soft-tissue plaque in the right carotid artery, 0.2 cm in thickness with the rest of the vessels being normal. ECHO showed left-ventricular diastolic dysfunction grade 1. Fungal culture and stain of

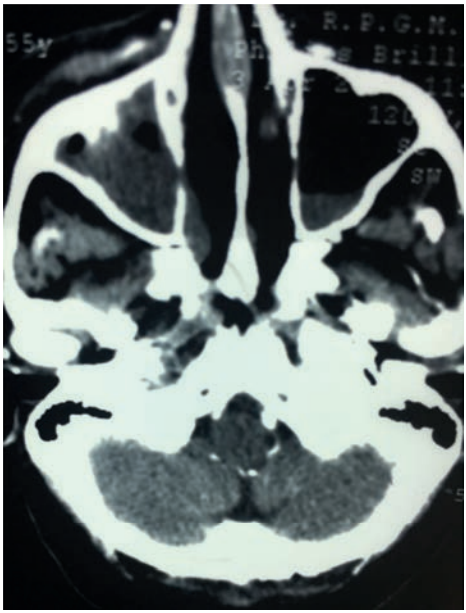

Fig. 1. CT scan of nose and paranasal sinuses showing opacification of the maxillary sinus, right side > left side.

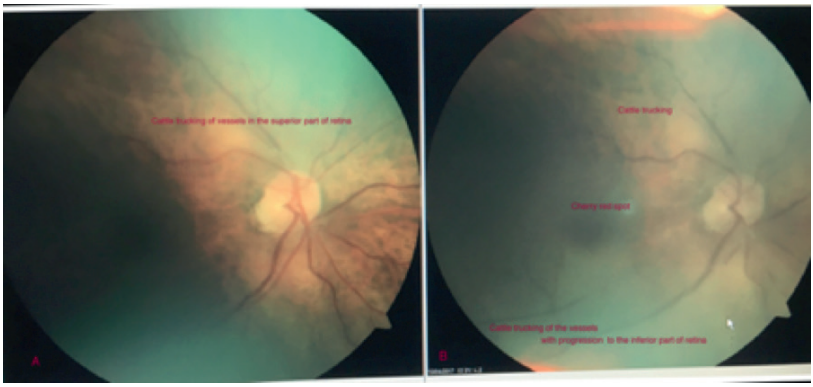

Fig. 2. Fundus photograph of right eye showing progression of ischemic changes in the retina. (Left) Cattle trucking of the vessels. (Right) Ischemic changes in the fundus.

pus from the sinus was negative. CT head revealed symmetrical prominence of the ventricular system.

On 12 April, 2017, she denied perception of light, and fundus of the right eye (Fig. 2) revealed increased cattle tracking along the vessels and a cherry-red spot at the macula. The chemosis in the right eye had increased, pupil in the right eye was non-reacting to light and ocular movements had restricted (Fig. 3).

Discussion

CRAO is mostly caused by a thrombus or embolus that leads to reduced blood perfusion of the retina.[4] It is a very rare complication of sinus surgery complicated with orbital cellulitis. It clinically presents as sudden painless acute unilateral or bilateral vision loss in the range of counting fingers to no light perception. The rate of spontaneously recanalization of the artery is about 15% with timely intervention.[5] The prognosis is very poor as only 61% of patients can regain a final VA of 6/120 or less.[3] One of the typical findings in CRAO is cherry-red spot that is found in about 90% of cases.

Sinus surgery leading to ophthalmic complications is not very common, despite the proximity of the orbit to the paranasal sinuses.[6] The most frequent complication of the Caldwell Luc operation is reported to be the paraesthesia or anaesthesia of the inferior orbital nerve. Blindness is a rare complication, which occurs due to direct trauma to the optic nerve or the pressure effect of an orbital haemorrhage.[7] Buus and co-workers detected orbital complications in only seven of their patients in a period of 10 years of their study.[6] Griffiths and Smith observed blindness and ocular motility disturbance in two patients following the Caldwell Luc procedure.[8] If retinal ischemia persists for more than 100 minutes, recovery of vision is unusual.[7]

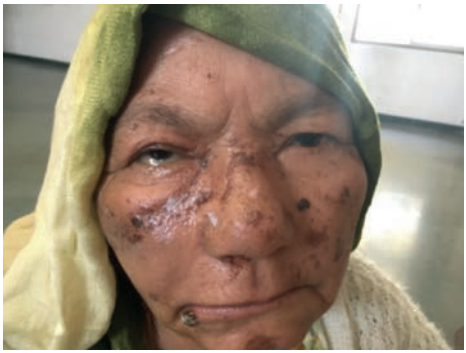

Fig. 3. Increased chemosis of the right eye with restriction of extraocular movements.

Many theories are given to explain the reason why CRAO occurs during surgical procedures. A prolonged hypotensive status with reduction in blood flow or increasing intraocular pressure including ocular compression during certain surgical procedures is associated with ocular ischemia,[8] which also causes ischemia of the retina, leading to CRAO and vision loss after surgery.

Ocular vascular damage during surgical maneuvers results in activation and aggregation of platelets and activated platelets release serotonin, which is a vasoconstrictor and induces a transient arterial spasm, causing transient or complete arterial occlusion, resulting in ischemia of retina leading to CRAO.[9]

Acute visual loss may be associated with acute sinusitis either secondary to complicated orbital cellulitis or as a part of the orbital apex syndrome. El-Sayed and Al-Muhaimeid[10] reported two cases of acute visual loss as a complication of orbital cellulitis due to sinusitis. One patient showed improvement in vision from hand motion to normal vision after intravenous treatment of pansinusitis and associated orbital cellulitis. The second patient recovered vision from no light perception to normal levels after exploration of the sphenoid and ethmoid sinuses along with intravenous antibiotics.

Slavin and Glaser[11] described three cases of sphenoethmoiditis causing permanent visual loss associated with minimal signs of orbital inflammation. This entity was called 'posterior orbital cellulitis'. Slavin and Glaser[11] defined it as a clinical syndrome in which early severe visual loss overshadows or precedes accompanying inflammatory orbital signs. Acute blindness may also result from orbital infarction syndrome. Orbital infarction is a disorder that may occur secondary to different mechanisms: (a) acute perfusion failure, common carotid artery occlusion; (b) systemic vasculitis and (c) orbital cellulitis with vasculitis, mucurmycosis.[11]

There is a critical time of 90 to 120 minutes after occlusion to perform interventions to improve vision; however, there is no approved modality to be effective

in the treatment of CRAO.[12] Immediate ocular massage and anterior chamber paracentesis, use of drugs such as intravenous acetazolamide and mannitol, inhalation of a mixture of 95% oxygen and 5% carbon dioxide (carbogen) are given to reduce IOP and improve blood flow to the eye.

Conclusion

Anatomic knowledge, proper evaluation, early recognition of complications and appropriate management of patients undergoing Caldwell Luc surgery will minimize these rare complications. Normally, orbital cellulitis responds to systemic antibiotic therapy and surgical drainage without signs of optic nerve compromise. We recommend that in all patients undergoing surgery by Caldwell Luc procedure, the ocular examination should be performed immediately after surgery, with a close follow up after the surgery to rule out the rare complication of CRAO, as delay in diagnosis and intervention could eventuate to severe vision loss.

Acknowledgements

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Isolated bilateral congenital lacrimal gland agenesis presenting as dry eye in childhood: a rare entity

Anitha Venugopal, Sowmya Peri, Ravi Chandra, Meenakshi Ravindran, Rengappa Ramakrishnan
Aravind Eye Hospital, Tirunelveli, Tamil Nadu, India

Abstract
We report the case of a 1-year-old child who presented with complaints of redness and defective vision since birth. The child had no systemic abnormalities. On examination, complete keratinization of the bulbar conjunctiva and cornea was noted with dry, lustreless and irregular surface. Corneal sensation was intact. Orbital MRI revealed bilateral agenesis of the lacrimal gland with normal salivary glands. The child was given vitamin supplementation, cyclosporine eye drops along with lubricants and tape tarsorrhaphy in the night. Permanent occlusion of both the lower puncta was done. There was decreased ocular surface congestion, with frequent wetting of the ocular surface, which continued in the months to follow. We present a case of isolated bilateral lacrimal gland agenesis with normal salivary glands, a rare cause of dry eye in children. An early diagnosis and conservative management can help in maintaining functional vision in such cases.

Keywords: *dry eye, keratinization, lacrimal gland agenesis, tarsorrhaphy*

Introduction

Congenital lacrimal gland agenesis is a rare presentation during childhood.[1,2] It may occur as an isolated condition or may be associated with salivary gland agenesis and atresia of the lacrimal gland drainage system.[3,4] We present here a 1-year-old boy with an isolated form of congenital bilateral lacrimal gland agenesis with normal salivary glands as one of the rare causes of dry eye in childhood.

Case report

An active, well-nourished, 1-year-old male child was presented at Aravind Eye Hospital, Tirunelveli by his parents in December 2013 with complaints of redness and defective and wandering vision since birth. The child was treated elsewhere as a case of bilateral corneal ulcer with topical antibiotics and lubricants for the last 1 month. The child was otherwise healthy with no systemic abnormalities.

Correspondence: Sowmya Peri, Aravind Eye Hospital, Tirunelveli, Tamil Nadu, India.
E-mail: sowmya.peri12@gmail.com

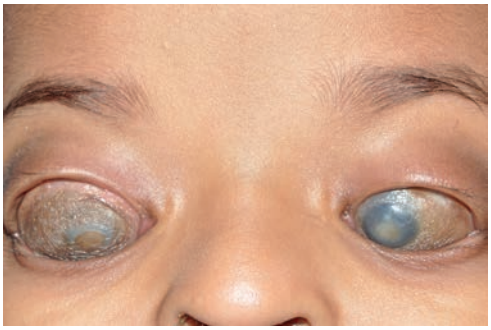
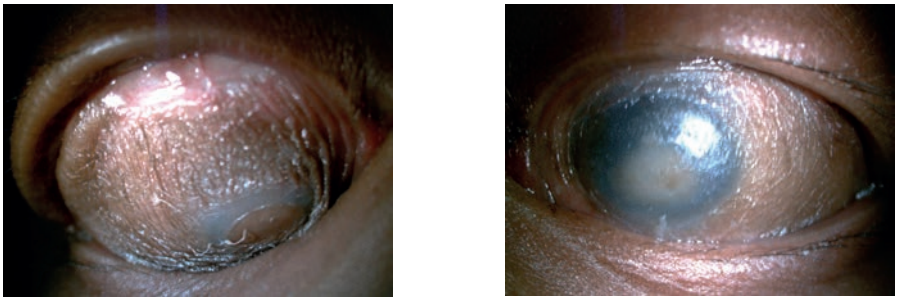


Fig. 1. Initial clinical photograph of the child showing bilateral complete keratinization of the bulbar conjunctiva and cornea with dry and irregular surface.



A B

Fig. 2. Slit lamp photographs of the right eye (A) and left eye (B) of the child.

There was no history of consanguinity of marriage among parents and no significant family history. TORCH profile was negative and karyotyping was normal.

On examination, the child was not able to fix light. Head posture was normal and no facial asymmetry was noted. Madarosis was noted in both eyes with hypertrophic upper lids. Cornea and conjunctiva were exposed with incomplete and reduced blink. Complete keratinization of the bulbar conjunctiva and cornea was noted with dry, irregular and lustreless surface (Figs. 1 and 2). Schirmer's test I and tear break up time could not be evaluated as the child was not cooperative. Corneal sensation was intact as checked by a wisp of cotton and confirmed with a Cochet–Bonnet aesthesiometer.

Examination under anaesthesia revealed normal corneal diameter in both eyes. Intraocular pressure was normal (as measured by Tonopen XL). Anterior lenticular opacity was seen in both eyes. Ultrasonography of both eyes was within normal limits.

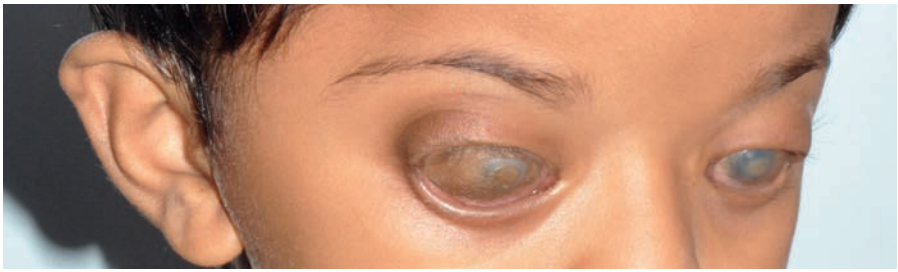


Fig. 3. Recent clinical photograph of the child showing decreased ocular surface congestion and increased wetting of ocular surface.

Orbital MRI revealed bilateral agenesis of the lacrimal gland with normal salivary glands. Conjunctival biopsy revealed squamous metaplasia with parakeratosis.

Systemic conditions that can cause dry eye syndrome were ruled out by testing for rheumatoid factor, ANA factor, purified protein derivative and angiotensin-converting enzyme titre. Chest X-ray was normal. The child was given intramuscular injections of vitamin A as per WHO guidelines, oral multivitamin syrups, frequent topical sodium hyaluronate drops, cyclosporine eye drops along with lubricants and tape tarsorrhaphy in the night. Permanent occlusion of both the lower puncta was performed. On follow-up visits, the child was able to fix and follow light in all directions. There was decreased ocular surface congestion, with frequent wetting of the ocular surface (Fig. 3). The child was advised to continue the same treatment with light stimulation and frequent follow-ups.

Discussion

Congenital lacrimal gland agenesis can be unilateral or bilateral. It can occur as an isolated condition or may be associated with salivary gland agenesis or atresia of the lacrimal gland system. The lacrimal gland begins to develop at the end of the second month of intrauterine life from the superolateral side of the conjunctival sac. Full differentiation of the lacrimal gland occurs only 3 to 4 years after birth. Hence, any disarrangement in these early stages may lead to lacrimal gland agenesis.

Chronic redness of the eyes, blepharospasm, absence of tearing and photophobia may indicate childhood dry eye syndrome. Systemic disorders such as Riley Day syndrome, Sjogren's syndrome, congenital bowel atresia leading to hypovitaminosis A and graft versus host disease following bone marrow transplantation[5] are some of the common associations of dry eye syndrome in childhood. Detailed patient history and systemic workup is necessary to find out the specific cause of dry eye syndrome.

Our patient showed bilateral lacrimal gland agenesis with normal salivary gland architecture in MRI. Also, the child had no systemic abnormalities. He had normal salivation and did not show any symptoms of dry mouth during subsequent follow-ups.

A review of the literature with respect to congenital lacrimal gland agenesis was done. Caccamise and Townes[3] reported absence of lacrimal puncta, congenital alacrima and lack of salivation in a 9-year-old child. Many case reports with respect to combined agenesis of lacrimal gland along with all salivary glands were reported by Milunsky et al.[1] and Ferreira et al.[4] Kim et al.[2] reported two cases of lacrimal gland agenesis in the same family in 2005. Autosomal dominant inheritance of congenital alacrima caused by hypoplasia of the lacrimal Gland was described by Mondino and Brown.[6] Autosomal-dominant conditions associated with lacrimal gland aplasia include lacrimo-auriculo-dento-digital syndrome and autosomal-dominant aplasia of lacrimal and salivary glands.[7] Mutations in genes encoding fibroblastic growth factor 10 were associated with aplasia of the lacrimal gland and salivary gland, as reported by Entesarian et al.[8]

This case emphasizes that bilateral congenital lacrimal gland agenesis should be considered as a rare cause of dry eye in childhood in an otherwise normal child, who presents with no significant systemic abnormalities. The improvement in ocular surface wetting after initiation of treatment may be related to the normally functioning accessory lacrimal glands of Krause and Wolfring. Non-invasive measures such as MRI help in the diagnosis of lacrimal gland agenesis. Early diagnosis and conservative management can help in maintaining functional vision.

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Macular buckle with Morin–Devin T implant for pathological myopia with macular hole

Abhishek Anand[1], Lalit Agarwal[2], Nisha Agrawal[3], Atul K. Anand[1]
[1]Vitreoretina Department, All India Institute of Medical Sciences, Patna, India;
[2]Vitreoretina Department, Biratnagar Eye Hospital, Biratnagar, Nepal;
[3]Cataract Department, Biratnagar Eye Hospital, Biratnagar, Nepal

Abstract

Introduction*: Pathological myopia is commonly associated with myopic traction maculopathy, which includes foveoschisis, foveal retinal detachment, macular hole (MH) and/or macular detachment (MD). Macular buckling is a rarely practiced extra-ocular surgical modality these days. The purpose of this study was to investigate the efficacy of primary buckling with Morin–Devin T implant for MD with MH and posterior staphyloma.*

Case description*: A 52-year-old female presented with light perception vision in her right eye with posterior staphyloma, localized neurosensory detachment, and MH. She underwent primary macular buckling with Morin–Devin T implant. During the immediate postoperative day the wedge indentation was found misaligned to the fovea. A revision surgery was done after 2 weeks for repositioning of the macular wedge. Spectral domain optical coherence tomography confirmed indentation at the MH with resolution of subretinal fluid and hole closure. Her BCVA was 2/60 at 3 months postoperative and it remained the same even at 6 months of follow-up.*

Conclusions: *Primary macular buckling can be an effective procedure in eyes with MH with detachment and posterior staphyloma with or without associated foveoschisis. Morin–Devin T implant placement is a relatively simple procedure with short surgical time and excellent outcome.*

Keywords: *macular buckling, Morin–Devin T implant, myopic foveoschisis*

Introduction

Pathological myopia with associated myopic traction maculopathy (MTM) is a relatively common posterior segment disease in the Asian population.[1] MTM includes foveoschisis, foveal retinal detachment, lamellar or full-thickness macular hole (MH), and/or macular detachment (MD)[2] and is generally associated with a posterior staphyloma.[3] OCT studies have shown frequent association of myopic foveoschisis with MH with or without retinal

Correspondence: Dr. Nisha Agrawal, Cataract Department, Biratnagar Eye Hospital, AtithiMarg, Rani, Biratnagar-17, Nepal.
E-mail: drnisha_agr@hotmail.com

detachment and the pathogenesis and management of the same has inspired much debate in the literature.[4]

Release of epiretinal traction by pars plana vitrectomy with or without internal limiting membrane (ILM) peeling with gas or silicon oil tamponade has enjoyed a reasonable success. However, pars plana vitrectomy (PPV) with ILM peeling in high myopic eyes is surgically challenging and is associated with a low rate of MH closure and frequent complications.[5,6] Scleral wall modulation by scleral shortening or episcleral buckling has been reported with good anatomical and functional results.[6,7]

Methods

Morin–Devin T implant {France Chirurgie Instrumentation (FCI), Paris, France}: Morin–Devin T implant has two components: a 4-mm wide silicone band and a 7-mm solid macular wedge (Fig. 1A). The T-shaped macular buckle is created by threading the band through the solid silicone macular wedge's planoconvex end (Morin–Devin "T"-shaped macular wedge).[8] The horizontal line of the "T" is formed by the solid silicon band and the vertical line of the "T" is formed by the macular wedge symbolically (Fig. 2). Although the indenting wedge end of the macular buckle is slightly convex on the non-indenting side but due to huge mismatch of convexity of the indenting and the non-indenting side, it would be more apt to call it planoconvex.

Surgical technique

180° temporal limbal peritomy was performed. Superior (SR), inferior (IR), and lateral recti (LR), and inferior oblique (IO) muscles were carefully isolated and secured by anchoring sutures using muscle hooks. Care was taken to secure all muscle fibers during IO isolation.

The 4-mm solid silicon band was first passed under the IR, IO, and LR. After passing underneath the LR, in the plane between the LR and the SR the 4-mm band was threaded through the slit provided in the indenting head of the macular wedge creating the T (Figs. 1B and 2).

The macular wedge indenting head along with the threaded silicon band was then negotiated under the LR. A long curved forceps holding the macular wedge tip was used to negotiate the macular wedge and to place the indentation of the planoconvex wedge under the detached MH carefully. Care must be taken so that the convex indenting face of the wedge faces the sclera while negotiating under the LR. Simultaneous indirect ophthalmoscopy with a +20 diopter lens was used to confirm the desired indentation. Care was taken while manipulating the

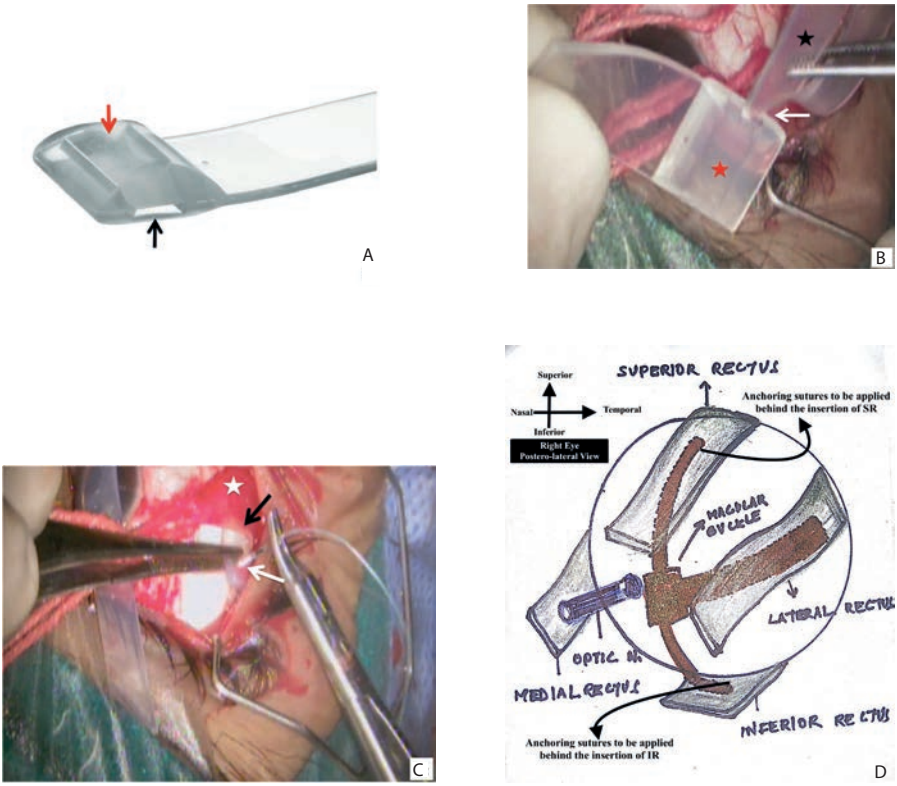

Fig. 1. Morin–Devin T Implant. (A) 7 mm solid macular wedge with biconvex end. "Red arrow" indicates the biconvex side of the macular edge, which will indent the macular area. "Black arrow" points to the slit in the solid macular wedge through which the silicon band will be threaded. (B) Creation of a T-shaped macular buckle by threading of a 4-mm silicone band through the solid silicone macular wedge's biconvex end (white arrow). "Black star" points to the solid 4-mm silicone band. "Red star" points to the solid macular wedge. (C) Anchoring of superior border of macular wedge with 5-0 Ethibond sutures to the sclera. "White star" indicates the lateral rectus (LR). Black arrow points to the superior border of the LR. White arrow points to the passing of the 5-0 Ethibond suture through the 7-mm macular wedge and being anchored to the sclera at the superior border of the LR. (D) Three-dimensional drawing of the right eye with Morin–Devin T implant from a posterolateral point of view. Free anterior ends of the 4-mm band secured just posteriorly beneath the insertion of the superior and inferior rectus, respectively. Free anterior end of the macular wedge secured to sclera just posterior and underneath the insertion of the LR.

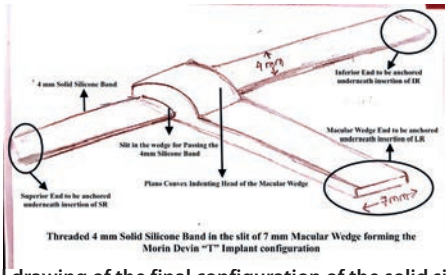

Fig. 2. Three-dimensional drawing of the final configuration of the solid silicone band and macular wedge after threading of the band into the slit provided at the indenting head of the wedge forming the "T" configuration.

wedge to the desired position so that inadvertent trauma to the optic nerve and short ciliary vessels could be avoided.

From our experience and from a literature search accurate positioning of the indenting head is very important. The indenting head once placed produces enough visible indentation at the macular area. The desired indentation to be achieved is the indenting bump should be slightly below the edge of staphylomatous excavation. Placement of the macular wedge is enough to achieve the desired indentation in most of the cases.

In cases of extreme staphyloma increasing the tension on the 4-mm solid silicone band can be used to increase the indentation.

The free anterior end of the macular wedge which formed the inferior end of the T was secured underneath the LR by anchoring its superior and inferior borders to the sclera with a 5-0 Ethibond suture. Three anchoring sutures were passed at the superior border and two at the inferior border of the 7-mm silicon macular wedge to prevent future displacement (Fig. 1C).

The 4 mm band was passed underneath the SR. The extra-long superior band was discarded and the cut end was secured nasal to the insertion of the SR with 5-0 Ethibond sutures. The inferior end of the 4-mm band was similarly fashioned and anchored nasal to the insertion of the IR. Tenon and conjunctiva were secured with a 8-0 polyglactin suture. The final position of the buckle with respect to the muscles is shown in Figure 1D.

In this case, only primary external macular buckling (PEMB) was performed. In cases of subrotal retinal detachment and especially detachment limited to the staphylomatous area or up to the vascular arcade, no drainage of subretinal fluid needs to be done. The macular fluid gets absorbed gradually. It may take few days to months for complete reabsorption of the fluid. In cases of extensive retinal detachment, subretinal fluid can be drained from a peripheral location. Air or gas tamponade can be used for the same. The available literature for PEMB has a success rate of around 90%.

Case summary

We report a case of a 52-year-old woman who had posterior staphyloma with MH and macular detachment limited to vascular arcade in the right eye (Fig. 3A). The patient underwent PEMB with Morin–Devin T implant as described above.

Postoperatively, however, the indentation of macular buckle was infero-temporal to the fovea. The patient underwent a revision buckling surgery after 2 weeks. Satisfactory results were obtained intraoperatively and postoperatively after the revision surgery (Fig. 3B).

At 3 months of follow-up, best corrected visual acuity (BCVA) improved to 2/60. SD-OCT showed significant buckle effect and resolution of MD with hole closure (Fig. 3C). A persistent restriction of eye movement on lateral gaze was noted at the last follow-up. The visual acuity remained static even at 6 months of follow-up.

Discussion

MTM in varying severity invariably coexists with posterior staphyloma. Progressive axial elongation along with anteroposterior vitreous traction and taut ILM creates shearing forces responsible for foveoschisis with or without MH and retinal detatchment.[2,9]

Various authors have reported significant success of pars plana vitrectomy with ILM peeling and tamponade in MTM.[5,10] Significant surgical expertise is required while working in an eye with abnormal scleral rigidity, longer axial length, mismatched instruments to axial length size, and visibly reduced contrast at the posterior pole due to myopic degeneration. Low MH closure rates,[5] development of extrafoveal holes,[6] progression of foveoschisis post ILM peeling[11] and redetachment post tamponade removal[6] mars its eventual success rate and its real success is questionable.

Macular buckling addresses the pathology by changing the configuration of the posterior pole from concave to planoconvex, thus relieving anteroposterior and tangential traction, scleroretinal mismatch and also reinforces the retinal

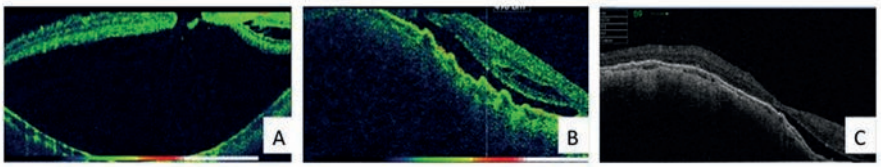

Fig. 3. SD-OCT showing reattachment after macular buckling with the Morin–Devin T implant. (A) Preoperative OCT showing macular hole with posterior ectasia of scleral wall. (B) One-month postoperative OCT showing persisting macular hole with significant indentation at the fovea. (C) Three-month follow-up showing closure of macular hole with persisting of detachment nasal to fovea.

pigment epithelium and neurosensory retina adherence by bringing them together in a chorioretinal atrophied area.

Although eclipsed by PPV for a long time, macular buckling has shown resurgence in recent times with reports coming from various centers emphasizing high success rates of macular buckling with or without vitrectomy.[6-8] In a case series reported by Ando F et al. comparing episcleral macular buckling (EMB) versus PPV in eyes with retinal detachment due to MH with posterior staphyloma, the retinal reattachment rate in EMB group was 93.3% after primary surgery and 100% after secondary surgery. In the PPV group, the retinal reattachment rate was 50% after primary surgery and 86% after secondary surgery using the EMB procedure, thus indicating a better anatomical success rate after primary EMB than after primary PPV.[12] Many case series with primary EMB or EMB with PPV have reported higher anatomical and functional success rate over primary PPV alone.[6-13]

Different macular buckles have been described in the literature. The most popular one is the Ando plombe explant (Ondeko Corporation Japan). It is a solid silicone rod with a metallic wire inside that allows it to be bent to obtain the desired buckling effect of the macular area. Mateo et al. coupled the indenting head to a 30-g optical fiber, which can be turned off and on, to help in accurate placement of the buckle by transillumination.[14]

Similar to the Ando plombe explant is the AJL macular buckle (AJL Ophthalmic Spain).[14] This buckle is made up of PMMA material covered with silicone to increase its biocompatibility. It has a spherical indentation head while the Ando plombe has an ellipsoidal head. In order to get optimum indentation, the arm length and curvature in AJL is customized to the individual's eye. AJL can also be coupled with optical fiber for guided placement using transillumination. Both Ando plombe and AJL can be easily placed by just exposing the supero-temporal quadrant and thus scores over other macular buckles.[7,14] However, indentation with the above buckles cannot be accurately titrated intraoperatively. The biggest deterrent is the cost of these explants in South Asia, which is almost 50–100 times more than the Morin–Devin T implant.

Another commonly used macular buckle is the adjustable macular buckle which has a solid silicone handle with a terminal plate for indentation.[15] The terminal plate has two winglets on either side for passing mersilene suture. The two ends of the suture are circumnavigated and tied in the opposite quadrant under the medial rectus. The indentation can be increased or decreased by tightening or loosening the suture postoperatively. The main disadvantages are longer learning curve and requirement of LR disinsertion for securing the explant under LR.[6,7]

Some authors have also reported use of solid silicone sponge with or without a metal wire (L-shaped macular buckle and wire-strengthened sponge exoplant).[15] However, long-term safety of the metal wire is not known and extrusion of sponge

is a real concern from these explants. Also intraoperative and postoperative titration is not possible. Suturing of silicone tire and sponge by direct visualization of the staphylomatous area has been used in the past but requires disinsertion of muscles for macular exposure and there lies the risk of perforation of the extremely thin staphylomatous area.[6,15]

Complexity of different procedures and unfamiliarity has dissuaded macular buckling becoming popular, especially in the Indian subcontinent. The Morin–Devin T implant scores a huge economic advantage. Unlike other procedures, the T implant does not require muscle disinsertion, posterior suture, and any open surgical access to posterior pole making the procedure relatively simple. Inherent disadvantages of macular buckle like intraoperative risk of scleral perforation, compromise of short posterior ciliary circulation, damage to ONH, abduction deficit, misalignment under the fovea, and late development of chorioretinal atrophy exist in T implants too.[8]

In our first attempt we had buckle misalignment. This can be prevented by using a customized curved forceps for placing the macular wedge, ability to differentiate false indentation produced by instrumentation, and better hand and eye coordination. Transillumination with an optical fiber has been used with other implants.[14] No such commercially available modifications are available with the Morin–Devin T implant. An extrapolation can be done by using a retaining suture to fix a fiber-optic cable at the macular wedge which can be used to confirm the macular indentation and later removed by pulling off the fiber-optic cable. In a previous study, a 25-g self-retaining chandelier endoilluminator along with a wide angle viewing system was used to confirm appropriate indentation.[13]

In our case, we achieved satisfactory chorioretinal apposition and closure of MH though with abduction deficit at 3-month follow-up on SD-OCT. We believe that MTM with coexisting pathology can be addressed with scleral wall reshaping using a relatively simple technique of macular buckling with the Morin–Devin T implant.

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Characteristics and treatment outcomes of patients with primary ocular adnexal lymphoma in Northern Thailand

Kasem Seresirikachorn[1], Sakarin Ausayakhun[1], Damrong Wiwatwongwana[1], Ponsak Mahanupab[2], Teerada Daroontum[2], Lalita Norasetthada[3]

[1]Department of Ophthalmology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand; [2]Department of Pathology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand; [3]Division of Hematology, Department of Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

Abstract

Purpose: *To assess the characteristics and treatment outcomes of patients with primary ocular adnexal lymphoma (OAL) in Northern Thailand.*

Design: *Retrospective cohort study.*

Methods: *Data was collected from electronic medical records and operative notes from Chiang Mai University Hospital between January 2009 and December 2014. All available tissue biopsies of 54 patients were reviewed by agreement of two pathologists. The clinical characteristics and treatment outcomes were collected and analyzed.*

Results: *A total number of 54 patients were identified of which 57.4% were female. The median age was 61.0 years (range, 4-86). The most common subtype of lymphoma was extranodal marginal zone lymphoma (ENMZL) of mucosa-associated lymphoid tissue (MALT) (n = 46, 85.2%). Seventy-five percent of the patients presented with a mass at the ocular adnexa, while 14.8% of the patients presented with proptosis. The sites of origin were as follows: lacrimal (46.3%), orbit (31.5%), conjunctiva (13%) and eyelid (7.4%). Two-thirds of the patients had Ann-Arbor Stage I, while 22% of patients had Stage IV. The majority of the patients (68.1%) had a low-risk international prognosis index (IPI). Treatment modalities involved field radiation (IFRT, 50%), chemotherapy (31.6%), combined chemoradiotherapy (7.9%) and surgical resection (10.5%). The overall response rate was 100% with a complete response rate of 77.8%. In patients with low-grade lymphoma, including MALT lymphoma, the 3-year progression-free survival (PFS) and overall survival were 69.9% and 92.5%, respectively.*

Conclusion: *ENMZL of MALT was the major subtype of primary OAL. Radiotherapy was an effective treatment for the lower stages of disease providing a high response rate and encouraging survival outcomes.*

Keywords: *extranodal marginal zone lymphoma of mucosal-associated lymphoid tissue, ocular adnexal lymphoma, radiotherapy, treatment modalities*

Correspondence: Kasem Seresirikachorn, MD, Department of Ophthalmology, Tambon Sripoom, Amphur Muang, 110 Inthawarorot Road, Chiang Mai, Thailand 50200.
E-mail: chimm_chimm@hotmail.com

Introduction

Primary ocular adnexal lymphoma (OAL) is the most common malignancy of the eye.[1] Primary OAL is defined as lymphoma that occurs at the conjunctiva, lacrimal apparatus, eyelid and in the orbit. OAL comprised 2% of non-Hodgkin lymphoma and 8% of extranodal lymphoma.[2] The most common subtype is extranodal marginal zone lymphoma (ENMZL) of mucosa-associated lymphoid tissue (MALT), which usually originates from B cells.[3,4] The most frequent site of origin is the orbit 40%, conjunctiva 35% to 40%, lacrimal apparatus 10% to 15% and eyelid 10%. The average age for diagnosis is from 50 to 70 years. Bilateral disease will be seen in 10% to 15%.[5]

Most of the patients (85-90%) were diagnosed with Ann-Arbor Stage I which responded very well to radiotherapy.[6] A complete response rate was 85% to 90%, and only 10% to 15% of the patients had Ann-Arbor Stage IV.[7,8] Currently, there are no standard treatment guidelines specifically for OAL. Patients were treated as ENMZL lymphoma in the other sites. Patients with Stage I disease were commonly treated with involved field radiotherapy.

The majority of previous reports were from Western countries. In Thailand, there were few publications regarding primary OAL.[9,10] To improve the diagnosis and quality of treatment in a patient with OAL, we conducted a retrospective review to study the characteristics and treatment outcomes of OAL patients in Northern Thailand.

Material and methods

This study was approved by the Institutional Review Board of Chiang Mai University Hospital, Chiang Mai, Thailand. The medical records and operative notes between January 2009 and December 2014 were reviewed to recruit patients with OAL. The inclusion criteria of patients in this study were patients diagnosed with OAL between January 2009 and December 2014 who had been followed for at least 1 year. The patients with follow-up of less than 1 year were excluded from the study. All available tissue biopsies of these patients were reviewed by two pathologists according to the 2008 World Health Organization guidelines. Immunohistochemical study routine was done to identify the subtype of lymphoma which included CD3, CD5, CD10 and CD20; however, because of the limitation of resource and available tissues, we cannot perform genetic study, but both of the experienced pathologists had a consensus agreement with the diagnosis with available tissues.

Data were collected including age at diagnosis, gender, underlying disease, clinical presentation, time to diagnosis, procedure of tissue biopsy, anatomical location, laterality, subtype of OAL, immunophenotype, Ann-Arbor staging, number of extranodal sites and performance status (ECOG). Additional data included serum

lactic dehydrogenase (LDH) level, anti-HIV, hepatitis B and C status, international prognostic index (IPI) and treatment modalities including type of chemotherapy, radiotherapy, response to treatment, recurrent status of disease, salvage therapy and current status of the patients. All treatment outcomes were evaluated for at least 1 year and disease activity was evaluated at the last time of follow-up.

Statistical analysis

The demographic and response rates were analyzed with descriptive statistics. Overall survival (OS) was measured from the date of diagnosis to the date of last follow-up or death from any cause. Progression-free survival (PFS) was calculated from the date of diagnosis to the date of last follow-up, second relapse/progression or death from any cause. Probabilities of OS and second PFS were estimated by using the Kaplan–Meier method and using log-rank test for survival comparison. All statistical analyses were performed using SPSS 16.0 for Windows (SPSS, Chicago, IL).

Results

Patients

Fifty-four patients were identified with primary OAL between January 2009 and December 2014. Demographic and clinical characteristics of primary OAL are summarized in Table 1. There were 31 females (57.4%) with a median age of 61 years (range, 4-86 years). The most common subtype of lymphoma was ENMZL of MALT (n = 46, 85.2%). Other histologic subtypes included diffuse large B-cell lymphoma (DLBCL, n = 3, 5.6%), peripheral T-cell lymphoma (PTCL, n = 3, 5.6%), MALT lymphoma with large cell transformation (n = 1) and small lymphocytic lymphoma (SLL, n = 1).

A palpable mass was the main presenting symptom (75.9%). Other manifestations were proptosis (14.8%), cellulitis (5.6%) and eye pain (3.7%). The median interval between onset of the first symptoms and the date of diagnosis was five months (range, 0.5-84 months). Anatomically the tumors were distributed as follows: lacrimal (46.3%), orbit (31.5%), conjunctiva (13%) and eyelid (7.4%). Most of the patients present with unilateral (75.9%). The primary immunophenotype was B-cell origin (94.4%).

At presentation, 32 (59.3%) patients had Ann-Arbor Stage I, six (12%) patients had Ann-Arbor Stage II, one patient had Ann-Arbor Stage III and 11 (22%) patients had Ann-Arbor Stage IV. Fifty-two patients (96.3%) had ECOG 0; therefore, the majority of patients with OAL were fully active and able to carry on all pre-disease activities without restriction.

Only two (4.8%) patients were previously diagnosed with HIV before presenting with primary OAL. The majority of the patients had a normal serum LDH level (94%) and lower-risk IPI (80.9%). There were few patients with HBV (n = 1) and HCV (n = 1) infection.

Table 1. Demographic and clinical characteristics of primary OAL

Characteristics	Number of patients (%)
Median age of diagnosis	61.0 years (range, 4-86)
Female	31 (57.4%)
Clinical presentation • Palpable mass • Proptosis • Cellulitis • Eye pain	 41 (75.9%) 8 (14.8%) 3 (5.6%) 2 (3.7%)
Median time to diagnosis	5.0 months (range, 0.5-84)
Anatomical location Lacrimal Orbit Conjunctiva Eyelid Lacrimal and conjunctiva	 25 (46.3%) 17 (31.5%) 7 (13%) 4 (7.4%) 1 (1.9%)
Laterality: Unilateral	41 (75.9%)
Subtype of lymphoma • MALT lymphoma • DLBCL • PTCL • MALT lymphoma with large cell transformation • SLL	 46 (85.2%) 3 (5.6%) 3 (5.6%) 1 (1.9%) 1 (1.9%)
Immunophenotype: B-cell origin	51 (94.4%)
Ann-Arbor staging • I • II • III • IV	 32 (64%) 6 (12%) 1 (2%) 11 (22%)
Performance status (ECOG) • 0 • 1	 52 (96.3%) 2 (3.7%)
IPI • Low risk • Low-intermediate risk • High-intermediate risk • High risk	 32 (68.1%) 6 (12.8%) 7 (14.9%) 2 (4.3%)

Characteristics	Number of patients (%)
LDH level: normal (<246)/high	45 (93.8%)/3 (6.2%)
HIV status: positive	2 (4.8%)
HBV infection: positive	1 (2.4%)
HCV infection: positive	1 (2.4%)

Treatment and outcomes

Treatment modalities were as follows: IFRT (50%), chemotherapy (31.6%), combined chemoradiotherapy (7.9%) and surgical resection (10.5%). The most common regimen for chemotherapy was CHOP which was comprised of cyclophosphamide, doxorubicin, vincristine and prednisolone (40%). The other regimens were CP (chlorambucil and prednisolone, 26.7%), CVP (cyclophosphamide, vincristine and prednisolone, 20%), and ALL protocol (n = 1)(Table 2).

Treatment outcomes were categorized according to the subtype and staging of lymphoma (Table 3). Indolent lymphoma included ENMZL of MALT and SLL, while aggressive lymphoma comprised of DLBCL, PTCL and MALT lymphoma with large cell transformation. The response rate after treatment in patients either with indolent and aggressive lymphoma was 100%. Eleven (20.4%) patients in this study had disease progression or relapse. The 3-year PFS and OS of patients with indolent lymphoma were 69.9 and 92.5%, respectively, which appeared to be better than of those with aggressive lymphoma (3-year PFS and OS of 42.9% [p = 0.12] and 42.9% [p < 0.0001]) (Fig. 1A and B).

Table 2. Treatment modalities

Treatment modalities	Watch and wait (n = 16)	Treatment (n = 38)
Radiotherapy		19 (50%)
Chemotherapy CHOP CVP CP ALL protocol		12 (31.6%) 5 3 3 1
Surgery		4 (7.9%)
Chemotherapy and radiotherapy		3 (10.5%)

Table 3. Treatment outcomes categorized according to subtype and staging of lymphoma

Type of lymphoma	Staging	N	OR (%) (CR, %)	3-year PFS (%)		3-year OS (%)	
Indolent lymphoma	I-II	26	100 (76.9)	70.2	69.9	96.8	92.5
	III-IV	5	100 (60)	55.6		50.0	
Aggressive lymphoma	I-II	3	100 (100)	33.3	42.9	33.3	42.9
	III-IV	2	100 (100)	66.7		66.7	

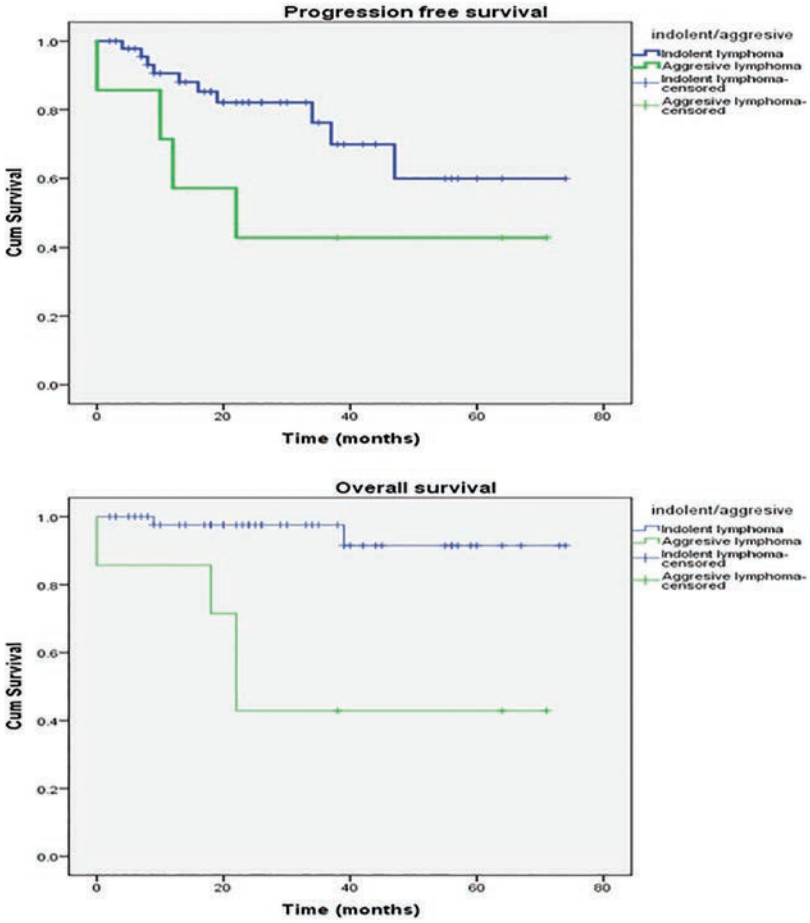

Fig. 1. (A) Kaplan–Meier PFS according to clinical subtypes of symptoms. (B) Kaplan–Meier OS according to clinical subtypes of lymphoma.

For patient with limited stage indolent lymphoma, either unilateral or bilateral ocular adnexal involvement had no significant effect on event-free survival (EFS) and OS, although patient with unilateral involvement had a trend of better EFS (median EFS was not reached) than those with bilateral involvement (EFS = 29 months, p = 0.025). Moreover, in this particular group patients, anatomical involvement had no effect on both EFS and OS (p = 0.66)

Among patients with indolent lymphoma, those with lower stages of disease had a superior 3-year PFS (70.2%) and 3-year OS (96.8%) than those with advanced stage disease with 3-year PFS and OS of 55.6% and 50%, respectively.

Discussion

Over the past decade, patients suspected to have primary OAL were transferred to Chiang Mai University Hospital, which is a tertiary care hospital in Northern Thailand. A multidisciplinary team was composed of an ophthalmologist, haematologist, pathologist and radiotherapists. With limited information on the patient treatment modalities and outcomes, it was difficult to explain to the patients regarding their disease status and prognosis. This study will provide a better understanding of patient characteristics and long-term outcomes after therapy.

The most common subtype of OAL in this study was ENMZL of MALT. Interestingly in our study, there was a higher proportion of patient of MALT lymphoma (85.2%) when compared with previous reports from the Asian and Western countries in which MALT lymphoma shows 30% to 70% of OAL[11-16] (Table 4). A palpable mass was the most common manifestation with a wide range of times from the first sign of symptoms to diagnosis of 0.5 to 84 months. This may be explained by the non-painful and slow progress of the disease. OAL commonly occurred in elderly patients which correlated with previous studies.[11-15,17-19]

Meunier *et al.*,[12] found that elevated LDH in low-grade lymphoma patients negatively predicted disease-free survival; however, in this series, most of the patients (93.8%) had a normal volume of LDH. Ferreri *et al.*[20,21] demonstrated an association between *Chlamydia psittaci* and OAL, but in our study, we have a limited number of tissues and methods to detect *C. psittaci*; therefore we did not find this association.

The most common site of origin was the lacrimal gland, which was different from previous studies,[12,14,16,17-19] but correlated with a previous study in Thailand.[10] Most of the patients had Ann-Arbor Stage I and radiotherapy was the first-line treatment option which concurred with previous reports.[12,14,15,17-19] Rituximab, anti-CD20 antibody, has been reported to have a good activity on OAL.[22-28] Due to its high cost, there was only one patient in this cohort who received rituximab with complete response after treatment.

In this study, an indolent subtype of primary OAL had an excellent outcome with a 3-year PFS and OS of 69.9% and 92.5%, respectively. Of these patients with indolent lymphoma, those with a limited stage had superior survival than those with advanced stage disease. Lymphoma is a chemo- and radio-sensitive disease; therefore, both aggressive and indolent lymphoma showed a good response rate after treatment. However, aggressive lymphoma nature had a high chance of progression and relapse disease afterward. Many studies from Western and Asian countries also showed similar outcomes with high PFS and OS after radiotherapy.[11,12,14,15,18,19]

This study had several limitations. First, it was retrospective in nature; therefore, there was a limitation in data collection. Second, ocular adnexa was not a common site of aggressive lymphoma, so we were not able to find a predicting prognosis factor in this subgroup of lymphoma. In the future, we should find a prognosis factor and association with *C. psittaci* in a larger study and focus on ENMZL of MALT which are the most common subtypes. The appropriate dosage of radiation and complications should also be further explored.

In conclusion, in Northern Thailand, ENMZL of MALT was the most common subtype of primary OAL. In a limited stage of disease, initial treatment with radiotherapy provided excellent outcomes.

Table 4. Characteristics and treatment outcomes of patients with OAL

Study	Country of study	N	Subtype of lymphoma, %	Clinical presentation, %	Anatomical location, %	Treatment modality,%	PFS, EFS, DFS, %	OS, %
This study	Thailand	54	MALT, 85.2% DLBCL, 5.6% PTCL, 5.6%	Palpable mass, 75.9% Proptosis, 14.8%	Lacrimal, 46.3% Orbit, 31.5% Conjunctiva, 13%	RT, 50% CT, 31.6%	PFS-3-LG, 69.9% PFS-3-HG, 42.9%	OS-3-LG, 92.5% OS-3-HG, 42.9%
Jenkins *et al.*[11]	Great Britain	192	MALT, 43% LPL, 23% FCL, 14%	NA	NA	NA	EFS-5-MALT,88% EFS-5-HG, 52%	NA
Coupland *et al.*[17]	Germany	136	All MALT	NA	Orbit, 40% Conjunctiva, 35% Eyelid, 18%	RT, 76%	NA	NA
Meunier *et al.*[12]	France	145	MALT, 36% LPL, 22% LL, 10%	Conjunctival lesion, 32% Exophthalmos, 27% Palpable mass, 19%	Orbit, 42% Conjunctiva, 35% Eyelid, 9%	RT, 68% RT+CT, 25%	EFS-5-LG, 68% EFS-5-HG, 43%	OS-5-LG, 78% OS-5-HG, 50%
Ferry *et al.*[13]	USA	353	MALT, 52% FCL, 23% DLBCL, 8%	Palpable mass, 69%	Soft tissue of orbit, 47.6%	NA	NA	NA

(continued)

Study	Country of study	N	Subtype of lymphoma, %	Clinical presentation, %	Anatomical location, %	Treatment modality,%	PFS, EFS, DFS, %	OS, %
Tanimoto *et al.*[18]	Japan	114	All MALT	NA	Orbit, 59% Conjunctiva, 36% Lacrimal, 3%	RT, 51%	EFS-5, 96% EFS-10, 57% EFS-15, 39%	OS-5, 96% OS-10, 92% OS-15, 71%
Bayraktar *et al.*[19] 2010	Great Britain	90	All MALT	Conjunctival, visible lesion Orbital and lacrimal, periorbital edema	Orbit, 46% Conjunctiva, 36% Lacrimal, 19%	RT, 85%	EFS-5, 73.6% EFS-10, 52.6%	NA
Portell *et al.*[14]	USA	95	MALT, 70.2% FCL, 14.9% DLBCL, 3.2%	NA	Orbit, 58.9% Conjunctiva, 41.1% Uvea, 18.9%	RT, 56% CT, 12%	NA	OS-5, 74.2%
Sniegowski *et al.*[15]	USA	82	MALT, 65.9% FCL, 14.6% DLBCL, 14.6%	NA	NA	RT, 34.1% CT, 32.9%	DFS-5, 55.9%	OS-5, 85.8%

N, number of cases; NA, not applicable
Lymphoma type: DLBCL, diffuse large B-cell lymphoma; FCL, follicle centre lymphoma; LL, lymphocytic lymphoma; LPL, lymphoplasmacytoid/lymphoplasmacytic lymphoma; MALT, mucosal-associated lymphoid tissue; PTCL, peripheral T-cell lymphoma
Treatment modalities: CT, chemotherapy; RT, radiotherapy
DFS-N, N-year disease-free survival; EFS-N, N-year event-free survival; PFS-N, N-year progression-free survival
HG, high-grade lymphoma, LG, low-grade lymphoma

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Evaluating the difference between autorefraction and subjective refraction may guide "fudge factor" for IOL power selection for cataract surgery after previous LASIK

Keith Ong[1,2,3,4,5], **Daisy Shu**[5,6]

[1]Department of Ophthalmology, Northern Clinical School, University of Sydney, Sydney, Australia; [2]Department of Ophthalmology, Royal North Shore Hospital, Sydney, Australia; [3]Department of Ophthalmology, Sydney Adventist Hospital, Sydney, Australia; [4]Department of Ophthalmology, Chatswood Private Hospital, Sydney, Australia; [5]Discipline of Anatomy & Histology, Bosch Institute, University of Sydney, Australia

Abstract

We propose a method to estimate "fudge factor" in the selection of IOL power for post-myopic LASIK patients undergoing cataract surgery by considering the difference between subjective refraction (SR) and autorefraction (AR) and to also compare the predictability of two popular regression formulae: SRK-T and Haigis.

Keywords: *autorefraction, cataract, IOL, LASIK, subjective refraction*

Introduction

The challenges associated with calculating accurate intraocular lens (IOL) power in eyes after laser in situ keratomileusis (LASIK) have been well documented.[1-5] It is common for patients to experience hyperopic "refractive surprise" in post-myopic LASIK based on standard regression formulae for IOL power determination.[3]

This imprecision in IOL calculation is caused by the inability to accurately measure the corneal power using topography or keratometry. Corneal power is determined using a topography or keratometry, which assumes that the power of the cornea's paracentral 3 to 4 mm does not significantly differ from that of the central cornea.[3] While this assumption is clinically acceptable for most normal eyes, it is no longer accurate for post-LASIK patients with abnormal corneal curvatures and results in inaccurate IOL power calculations.

Correspondence: Dr Keith Ong, 2 Railway Avenue, Eastwood, NSW 2122, Australia.
E-mail: keithong@optusnet.com.au

Report

Many methods have been proposed for the determination of IOL power in post-LASIK patients with mixed success, due to variability of the amount of LASIK correction done and corneal curvature changes of the thinner cornea over time. In this small study, we propose a method to estimate "fudge factor" in the selection of IOL power for post-myopic LASIK patients undergoing cataract surgery by considering the difference between subjective refraction (SR) and autorefraction (AR) and to also compare the predictability of two popular regression formulae: SRK-T and Haigis. The Haigis-L formula was not used as it already had a fairly constant fudge factor built-in to compensate for the reduced central corneal curvature of the post-op myopic LASIK cornea.

A retrospective case analysis was conducted on 10 consecutive eyes of seven patients with history of LASIK for myopia who underwent phacoemulsification with implantation of Alcon SN60WF posterior chamber intraocular lens from 2007 to 2013. The difference between AR and SR was compared post-cataract surgery, and the predictability of SRK-T and Haigis IOL power calculation formulae was evaluated by comparing the post-cataract surgery SR and AR to the refraction predicted by the formulae. Zeiss IOL Master 500 (Carl Zeiss Meditec, Jena, Germany) was used for biometry and IOL power calculation. The autorefractor used was Topcon RM3300 (Topcon Corporation, Japan).

Post-cataract surgery AR was significantly more minus than SR (spherical equivalent [SE] ± SD, 0.60 ± 0.44D, $p < 0.05$). The amount of LASIK correction showed a weak positive correlation with the difference between post-cataract surgery SR and AR, which was not statistically significant ($r = 0.63$). The difference between predicted refraction and post-cataract surgery AR was significantly less ($p < 0.05$) when calculated with Haigis (−0.061 ± 0.68D) in comparison to SRK-T (−0.65 ± 0.66D). There was also a significant difference ($p < 0.05$) between predicted refractions and post-cataract surgery SR when calculated with Haigis (−0.54 ± 0.66D) in comparison to SRK-T (−1.25 ± 0.76D).

AR with the Topcon autorefractor yields a more minus refraction in comparison to SR following LASIK. Post-cataract surgery in these eyes, AR also yields a more minus refraction in comparison to SR and the difference is fairly similar for a particular eye. Both SRK-T and Haigis formulae were more accurate in predicting post-cataract surgery AR than SR, and the difference between AR and SR is quite similar pre- and post-cataract surgery for a particular eye using the Topcon RM3300 autorefractor and Zeiss IOL Master 500. A different autorefractor and optical biometry instrument may yield a different fudge factor. Hence, this difference between AR and SR can be used as a guide for "fudge factor" when selecting the IOL power to achieve target SR.

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Original Article

Vision-threatening diabetic retinopathy necessitating vitrectomy in a tertiary care hospital in coastal Karnataka, South India

Narasimha Vasista Reddy, Yogish Subraya Kamath, Lavanya G. Rao, Krishna Addoor Rao, Shailaja Bhat Shenoy, Sulatha V. Bhandary
Department of Ophthalmology, Kasturba Medical College-Manipal, Manipal Academy of Higher Education, Karnataka, India

Abstract

Background: *The proportion of diabetic patients having vision-threatening diabetic retinopathy and those needing to undergo vitrectomy was documented.*

Methods: *A cross-sectional observational study was conducted at a tertiary care hospital in coastal Karnataka, South India. All patients with diabetes mellitus visiting the ophthalmology department in the study period were screened for retinopathy, and the data regarding the presence of maculopathy and proliferative retinopathy were included as vision-threatening retinopathy.*

Results: *Of the 1,435 diabetic patients included, 38.4% had retinopathy changes due to diabetes, with 8.71% having vision-threatening retinopathy and 1.81% needing vitrectomy.*

Conclusion: *Although the proportion of vision-threatening retinopathy is small, the rapidly increasing diabetic population requires the setting up of more resources for tackling this condition, at least at the tertiary levels of the health-care system. However, considering the increased human and economic resources involved in setting up vitrectomy units, more emphasis on strengthening screening programs for early detection and referral to reduce the progression of retinopathy to advanced stages would be appropriate.*

Keywords: *diabetic retinopathy, India, proliferative, tertiary care centers, vitrectomy, vitreoretinopathy*

Introduction

Diabetic retinopathy (DR) accounts for 1% of the blindness in the world.[1] Visual loss results from proliferative diabetic retinopathy (PDR) with vitreous hemorrhage, PDR with tractional retinal detachment (TRD), or macular edema seen in any stage.[2] Such stages have been termed sight or vision-threatening diabetic

Correspondence: Dr. Yogish Subraya Kamath, Associate Professor, Department of Ophthalmology, Kasturba Medical College- Manipal, Manipal Academy of Higher Education, Madhav Nagar, Manipal-576104, Karnataka, India.
E-mail: dryogishkamath@yahoo.co.in

retinopathy (VTDR). VTDR can be managed by methods including laser photocoagulation, anti-vascular endothelial growth factor (anti-VEGF) injections, and surgical techniques involving vitrectomy.[2,3] Although the former two modalities can be done as an outpatient procedure or in any sterile ophthalmic operating theater, vitreoretinal surgery can only be performed in a specialized operating room with specific and expensive equipment. This study attempts to document the number of VTDR patients who required vitrectomy at a tertiary care hospital in coastal Karnataka, South India. An understanding of the number of VTDR patients requiring vitrectomy would enable proper infrastructural planning and budget allocation, in an effort to tackle the burden of DR.

Methods

This was a cross-sectional hospital-based study conducted in a tertiary care multispecialty hospital in coastal Karnataka, South India, between November 2011 and April 2013.

The study was conducted in accordance with the Declaration of Helsinki. Institutional ethical committee was taken prior to the commencement of the study.

All patients with diabetes mellitus visiting the ophthalmology department were included. Diabetes was defined as fasting blood glucose of >110mg% and/or postprandial glucose of >140 mg% and/or glycated hemoglobin (HbA1C) of >6.5% and/or a history of treatment with antidiabetic medication. An informed consent of the patients was obtained before including them in the study.

All the patients underwent an ophthalmological evaluation that included an assessment of visual acuity with the Snellen chart, slit lamp biomicroscopic evaluation of the anterior segment, and intraocular pressure evaluation. Patients then underwent pupillary dilation with tropicamide 1% eye drops. The retinal evaluation was done by an ophthalmologist using +90 D lens on a slit lamp biomicroscope and indirect ophthalmoscopy in some cases. All patients with evidence of any retinopathy were examined by ophthalmologists specializing in retinal diseases. The DR classification was adopted as per the modified Airlie House classification system used in Early Treatment Diabetic Retinopathy Study. Macular edema that was clinically significant was included as maculopathy. The details of investigations and any subsequent ophthalmological interventions were retrieved and analyzed from the medical records of patients.

VTDR was defined as the presence of any nonproliferative diabetic retinopathy (NPDR) with macular edema and all cases of PDR. The patients in whom vitrectomy was indicated included those with

- Nonclearing vitreous hemorrhage of one-month duration, if they had not undergone pan-retinal photocoagulation (PRP) previously;

- Non-clearing vitreous hemorrhage of three-month duration, if they had undergone PRP previously;
- Recurrent vitreous hemorrhage;
- Progressive fibrovascular proliferation;
- TRD involving macula;
- Macular edema associated with taut posterior hyaloid membrane; and
- Neovascular glaucoma as a consequence of PDR with some visual potential.

Patients with vitreous hemorrhage, TRD, macular edema, and neovascular glaucoma due to causes other than diabetes were excluded.

The data collected were analyzed using SPSS, version 16.0**.** For statistical analysis, data were summarized using frequency and percentage for categorical variables.

Table 1. The number and percentage of patients with various types of retinopathy

Type of retinopathy	Number of patients (n)	Percentage
Mild NPDR	116	8.08
Moderate NPDR	191	13.31
Severe NPDR	96	6.68
Very severe NPDR	23	1.60
NPDR with maculopathy	49	3.41
PDR	63	4.39
PDR + maculopathy	13	0.9
Total DR	551	38.4
No DR	884	61.6
Total patients	1,435	100

Results

There were 1,435 diabetic patients included in the study, of whom 66.57% were males. Majority of them (88.49%) were in the age group of 31 to 70 years. DR changes were absent in 61.60% patients. The number and percentile of patients with the various types of DR are given in Table 1.

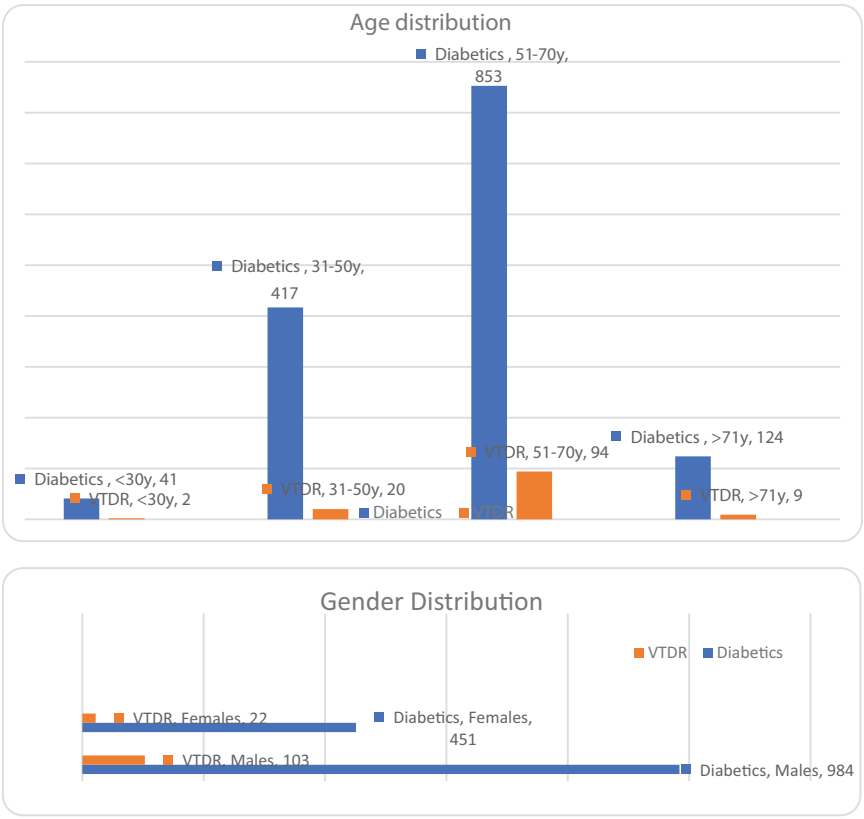

Fig. 1. Age and gender distribution of patients with VTDR.

The total number of patients with VTDR were 125 (8.71%). Figure 1 depicts the comparison of age and gender distribution of the VTDR patients among diabetics. Among the patients with VTDR, vitrectomy was indicated and advised in 26 patients (1.81%).

Discussion

This study documents the number of VTDR patients requiring surgical intervention. With the increasing numbers of patients with diabetes mellitus in the world, data on the regional prevalence of DR become important for planning the management strategy. Although the initial stages of DR require merely observation and systemic glycemic control, advanced stages of vision-threatening retinopathy require more intensive management.[2] The major modalities of

managing PDR include retinal photocoagulation, intravitreal anti-VEGF injections, and, in certain cases, vitreoretinal surgery.[4] The infrastructural and human resources needed for managing advanced retinopathy are limited. The expenses involved in the establishment of the needed resources for screening and management of DR are also high. Hence, a reliable estimation of the disease burden would help in the proper allocation of the limited resources to ensure optimal utilization. Only a small portion of patients would need surgical intervention for the management of VTDR, especially in cases of vitreous hemorrhage or retinal detachment. The hospital-based setup of our study was a limiting factor in determining the prevalence of VTDR. However, we felt that data regarding patients with VTDR requiring surgical therapy were more likely to be obtained from a tertiary care hospital providing vitreoretinal services.

In our study, DR was seen in 38.4% of diabetic patients. This was marginally higher than a 33.9% prevalence in another hospital-based study from Western India[5] and considerably higher than 20.4% reported in a population-based prevalence study in South India.[6] However, it was closer to the 45% prevalence reported in the South Asian community settled in the United Kingdom by Raymond *et al.*[7]

PDR was seen in 5.29% of diabetics in this study with NPDR in 33.08% patients. The proportion of retinopathy detection was higher than other studies and there were more NPDR cases detected in our study.[5,6] The difficulty in the detailed clinical screening of retinopathy in population-based studies may affect the accurate staging, especially of early stages. This factor may affect the prevalence values.[8] The use of fundus photography and evaluation can overcome this hurdle but is expensive for use in developing countries.[6] Our study probably was able to detect more retinopathy due to a detailed stereoscopic fundus evaluation of all patients, as well as the availability of confirmation by a specialist in doubtful cases. Poor retinopathy detection and management have been attributed to the lack of a specialist retina service.[9]

Many of the patients visiting our hospital had other systemic diabetic complications. The presence of retinopathy is known to be higher in the presence of coexisting microvasculopathies of other systems.[10] Hence, referral from these departments may also have accounted for a higher prevalence in our study.

We found that VTDR was present in 8.71% of the diabetics. Most of the patients with VTDR (91.2%) were in the age group of 31 to 70 years and 81.4% were males. Nearly 60% of these patients were in the working age group of 25 to 60 years. This implies that not only is there a threat of severe visual loss in almost 5.15% of all the diabetic patients in our study but that it will affect the potential breadwinners of their families. DR is known to be the leading cause of preventable blindness in the working adult population in the United States as well.[11]

Although the total DR percentage in our study is similar to the study by Raymond *et al.*, the proportion of VTDR is lesser (8.71% compared with 16% noted by Raymond *et al.*)[7] This may be attributed to the exclusion of severe NPDR without significant macular edema as vision threatening in our study.

We observed more males presenting with DR (68.57%) as well as VTDR (81.4%) compared with females. Other epidemiological studies[12,13] and reviews[14] have also observed a male predominance in DR.

Among the 125 patients with VTDR, vitrectomy was indicated in 26 patients. These accounted for nearly 1.81% of our diabetic study population. The benefits of vitrectomy in PDR were initially suggested by the Diabetic Retinopathy Vitrectomy Study (DRVS), and subsequent studies have strengthened this concept.[15,16] The technological advancements in surgical approach are probably the main factors responsible for this improved outcome.[16] However, such improved operating systems demand more elaborate and stringent operation theatres and surgical instruments.

In recent years, though, there has also been a decline in the rates of vitrectomy needed for DR management in some countries, due to an overall decrease in advanced stages of diabetic eye disease. This has been achieved due to an extensive and meticulous screening, early detection, and treatment program by these countries.[17] In addition to this, better dietary habits, lifestyle modification, and systemic therapy for glycemic control have probably contributed to lessening the rates of end-organ damage due to diabetes, including retinopathy.[18]

Hence, in countries with fewer resources but a high load of diabetic patients, systemic control of the disease by dietary and medical means should be emphasized. The improvement of screening programs for early detection of retinopathy patients would avoid progression to advanced stages. The use of teleophthalmology and telemedicine services can improve this endeavor.[19] Referral services to tertiary care centers providing integrated and complete care for diabetes and its complications can then be facilitated.

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Original Article

Intermediate-term outcome of placement of Baerveldt glaucoma implant for refractory glaucoma in a Malaysian population

Clarissa Ern Hui Fang, Seng Kheong Fang
Department of Ophthalmology, International Specialist Eye Centre, Kuala Lumpur, Malaysia

Abstract

Objective: *To report baseline characteristics and surgical outcomes of placement of Baerveldt glaucoma implant (BGI) in Asian eyes with considerably elevated intraocular pressure (IOP) despite maximal medical therapy.*

Design: *Retrospective case series of surgical cases from a single surgeon. Retrospective review of medical records of last clinic visits.*

Participants: *One hundred and ninety-seven eyes of patients underwent placement of 350-mm^2 Baerveldt implant.*

Methods: *The medical records of consecutive patients who underwent placement of a Baerveldt 350-mm^2 glaucoma drainage device (GDD) at the International Specialist Eye Centre from 2007 to 2014 were reviewed. Patients with a minimum 1-year follow-up were included. Baseline characteristics, pre-operative and post-operative IOP, number of glaucoma medications, visual acuity (VA) and complications were recorded. The pre-operative IOP is compared with the IOP at 1, 2, 3 and 5 years.*

Measures: *The IOP, VA, supplemental medical therapy, complications and success and failures were recorded.*

Results: *One hundred and ninety-seven patients were followed up at 1-year post-operation, 157 patients at 2 years, 120 at 3 years and 37 at 5 years. The mean baseline IOP of 29.2 ± 10.6 mmHg was significantly reduced at all time points post-operatively. Mean number of glaucoma medications was significantly lower at last follow-up than pre-operatively (1.8 vs. 2.7).*

Conclusions: *Placement of GDDs effectively reduces IOP without much long-term complication and may be useful in glaucomatous eyes with considerably elevated pre-operative IOP not well controlled with maximal medical therapy in the Asian population.*

Keywords: *Baerveldt implant, glaucoma, Malaysia, surgical outcomes*

Correspondence: Clarissa Ern Hui Fang, Level 8, Centrepoint South, The Boulevard, Mid Valley City, 59200 Kuala Lumpur, Federal Territory of Kuala Lumpur, Malaysia.
E-mail: fangclarissa@gmail.com

Introduction

Glaucoma drainage implants are commonly used in the surgical management of glaucoma. Traditional indications are those with refractory or complicated glaucoma such as neovascular glaucoma, aphakic, pseudophakic, post-silicone oil glaucoma, previous multiple surgeries and previous failed trabeculectomy. With the results of the tube versus trabeculectomy,[1] it is now being used earlier and may even be indicated as a primary treatment in certain cases. An example of a well-known glaucoma drainage device (GDD) is the Baerveldt glaucoma implant (BGI), a tube inserted into the anterior chamber and connected to a plate placed at the equatorial region. Success rates of such BGIs range from 60% to 93% at follow-up intervals between 14 and 37 months.[2] However, many studies are on Caucasian eyes and GDDs are equally important in Asian eyes. Asian eyes tend to have increased scarring and fibrosis, thus may have potentially higher failure rate.[3-5] The aim of this study was to determine the intermediate outcome of BGI surgery in Asian eyes performed in a tertiary centre in Malaysia.

Materials and methods

Patients

A retrospective review by computerized search of all patients at International Specialist Eye Centre (ISEC) Kuala Lumpur, Malaysia was carried out to identify those who underwent GDD surgery. The medical records of patients who underwent placement of a Baerveldt 350-mm^2 GDD from 2007 to 2014 were reviewed. Patients with a minimum 1-year follow-up were included. Baseline characteristics, pre-operative and post-operative intraocular pressure (IOP), number of glaucoma medications, visual acuity (VA) and complications were recorded. The pre-operative IOP was compared with the IOP at 1, 2, 3 and 5 years.

Procedure

The 350-mm^2 BGI model was used in all surgeries. As the procedure was performed by a single surgeon, the procedure and the pre-operative and post-operative management were similar in each case. Most procedures, 148(75.1%), were done under local anaesthesia, which was given as peribulbar injections with or without sedation, and the rest, 49(24.9%), were done under general anaesthesia. Of those under local anaesthesia, all were given peribulbar injection. In some, when the peribulbar anaesthesia was not adequate, they were supplemented with sub-Tenon's injection. The preferred quadrant for surgery was supero-temporal, then supero-nasal (if there was no Baerveldt implant supero-temporally), then infero-nasal and lastly infero-temporal (to avoid vortex veins and inferior oblique muscles). Anterior chamber paracentesis

was performed at the beginning of the surgery and slow aqueous release was performed (care especially with patients with neovascular glaucoma, and to prevent bleeding, viscoelastics may be instilled at this stage into the anterior chamber) Fornix-based conjunctival peritomy was performed, the Tenon's capsule separated and the appropriate muscle isolated and slung with a muscle hook. Mitomycin C (MMC) 0.02% soaked with Weck-Cel sponge was routinely placed under the sclera and Tenon's capsule for 3 minutes and washed away with copious amount of balanced salt solution (BSS). Haemostasis was secured with diathermy.

The BGI was primed to make sure the tube is patent and the plate placed under the appropriate muscle on each side and anchored with 8-0 nylon through each anchoring hole. The tube was ligated completely near its junction with the plate with 7-0 Vicryl using two throws. Care was ensured that there was no flow through this ligature. Then, at least 12 and up to 20 Sherwood venting slits were created through the tube distal to the ligature with the needle of the 7-0 Vicryl suture. The tube was then shortened and the length adjusted to be inserted about 2.5 to 3 mm into the anterior chamber. A tract was made through the sclera about 2 mm away from the limbus and entered into the anterior chamber through the angle. Care was taken that this tract was not too close to the iris and not too close to the cornea. A small amount of viscoelastics was instilled through the tract to make sure there is adequate space for the tube to be inserted. The tube was then inserted into the anterior chamber through this tract using a tube introducing forceps and the length was checked to be adequate. The tube was then anchored to the sclera with a mattress non-absorbable 10-0 nylon suture. The exposed area of the tube was then covered with donor cornea sclera (earlier preserved in glycerine, but subsequently soaked in BSS and then gentamicin eye drops) sutured with 10-0 nylon. The overlying conjunctiva was then closed with continuous absorbable 8-0 Vicryl stitch making sure the closure was watertight. Intracameral and topical antibiotic (moxifloxacin) was instilled and also topical Tobradex (dexamethasone-tobramycin combination) eye ointment (Alcon). The operated eye was padded and protected with a shield.

There were a few cases that were combined with cataract surgery with intraocular lens implant. In these cases, first the plate was inserted and then temporal clear cornea phacoemulsification cataract surgery was done with implantation of intraocular lens. Usually a single 10-0 nylon was applied to the clear cornea wound. Then finally the tube was inserted.

Patients were examined on the first post-operative day and 1 to 2 weekly (for 6 weeks) and then 1 to 3 monthly as clinically indicated. The IOP was measured with a Goldmann applanation tonometer at each visit, and glaucoma medication was added as required to supplement IOP reduction if the target IOP was

not achieved. A few cases had laser suture lysis on average of 4 to 5 weeks post-operatively if medications were not able to control the IOP.

Outcome criteria

The surgical outcome (at last visit) was assessed in terms of IOP, VA, and the incidence of complications. The IOP at last visit was recorded. A complete success was defined as IOP of between 6 and 21 mmHg without medication, qualified success as IOP between 6 and 21 mmHg with one or more medications and failure as IOP more than 21 mmHg or less than 6 mmHg and those who lost light perception.

Results

A total of 240 patients had the BGI surgery from 2007 to 2014. Patients with less than 12-months follow-up were excluded from this study. A total of 197 patients had 1-year follow-up post-operation, 157 patients at 2 years, 120 patients at 3 years and 37 patients at 5 years.

Table 1. Demographic characteristics of patients undergoing BGI surgery

Patients	**Total, n = 197**
Age	53.6 ± 17.8 years (range: 6-86)
<20 years	9 (4.6%)
>50 years	132 (67%)
Sex	
Male	141 (71.6%)
Female	56 (28.4%)
Ethnicity	
Chinese	142 (72.1%)
Malay	38 (19.3%)
Indian	15 (7.6%)
Other	2 (1.0%)
Operated eye	
Right	105 (53.3%)
Left	92 (46.7%)

All the patients were of Asian origin. The majority of the patients were from Malaysia (94.4%) and the rest were from Indonesia, Singapore and Saudi Arabia.

The patients consisted of 142 Chinese (72.1%), 38 Malays (19.3%), 15 Indians (7.6%) and 2 other (1.0%). The demographic features of the patients are summarized in Table 1.

The most common diagnosis for surgery was neovascular glaucoma; there were 51 eyes (25.9%). Neovascular glaucoma is prevalent because diabetes is very common in Malaysia and ISEC is tertiary referral centre. Many of the eyes with proliferative diabetic retinopathy have had previous intra-vitreal anti-VEGF or laser photocoagulation with signs of regression of the neovascularization before BGI surgery. However, some patients with poor media that precluded laser therapy or IOP too high with maximal medical therapy either underwent pre-operative intra-vitreal anti-VEGF or concomitant intra-operative intra-vitreal anti-VEGF and BGI. The second most common diagnosis was pseudophakia or aphakia in 48 eyes

Table 2. Primary pre-operative diagnosis of patients undergoing BGI surgery

Type of glaucoma	
Neovascular glaucoma	51
Pseudophakia/aphakia	48
Primary open-angle glaucoma with previous failed trabeculectomy	37
Uveitic glaucoma	19
Post-keratoplasty	10
Juvenile	7
Post-traumatic	5
Steroid-induced	5
Congenital	4
Post-retinal detachment	3
Iridocorneal endothelial syndrome	3
Primary angle closure	2
Sturge-Weber syndrome	1
Silicone oil glaucoma	1
Pseudoexfoliation	1

(24.4%), mostly after complicated cataract surgery. BGI was the primary procedure for those refractory cases such as neovascular, uveitic, post-retinal detachment (RD)/silicone oil, post-corneal graft, some pseudophakic/aphakic and iridocorneal endothelial syndrome. The primary pre-operative diagnoses are listed in Table 2.

Table 3 summarizes the mean IOP before and after BGI surgery at 1, 2, 3 and 5 years. IOP was reduced from a mean pre-operative IOP of 29.2 ± 10.6 to 14.7 ± 4.4 after 1 year, a reduction of approximately 49.7%. After 2 years, the mean IOP was 14.4 ± 4.4 (50.7% reduction), after 3 years it was 15.0 ± 3.9 and after 5 years it was 15.5 ± 4.3. Student's paired t-tests were carried out which showed that there is a difference between pre-operative IOP and post-operative IOP. The p-value is 0.0001 in all comparisons, showing that the difference is significant. This is shown in Table 4.

Overall outcomes for BGI in terms of IOP: 47 eyes (23.9%) were classified as complete successes, 144 eyes (73.1%) were qualified successes as they continued medication to control the IOP and 6 (3.0%) were failures. Of the failures, two eyes (1%) had no perception to light; four eyes (1.5%) had IOP levels more than 21 mmHg, which had further glaucoma surgeries; three eyes had second glaucoma implants and one eye had transscleral cyclophotocoagulation. Table 5 summarises the overall outcomes for BGI.

Table 3. IOP before and after BGI surgery

IOP	Mean(SD)	N
Pre-operation	29.2(10.6)	197
1 year	14.7(4.4)	197
2 years	14.4(4.4)	158
3 years	15.0(3.9)	120
5 years	15.5(4.3)	37

Table 4. IOP comparisons before and after BGI surgery

Pre-operation IOP compared to	Paired differences mean	P-value	95% Confidence interval
IOP at 1 year	14.4	0.0001	12.8603-16.0128
IOP at 2 year	14.3	0.0001	12.5779-16.0677
IOP at 3 year	14.6	0.0001	12.6028-16.6138
IOP at 5 year	14.6	0.0001	11.3983-17.8450

Table 5. Overall outcome for BGI surgery

Outcome at last visit	
Complete success (IOP 6-21 mmHg; no medication: not NPL)	47 (23.9%)
Qualified success (IOP 6-21 mmHg; with medication: not NPL)	144 (73.1%)
Failure IOP > 21 mmHg, IOP < 6 mmHg NPL at last visit	6 (3.0%)

NPL, no perception to light

Table 6. Post-operative VA outcomes of BGI surgery

VA	1 year	2 years	3 years	5 years
Improved[a]	34.5%	34.3%	27.0%	26.3%
Unchanged	34.5%	38.2%	27.0%	31.6%
Worsened[a]	31.0%	27.7%	45.9%	42.1%

[a]By one or more lines of Snellen acuity

Table 6 summarises the change in VA. The VA at clinic visit was compared to pre-operative VA. There was an improvement of VA in most patients after 1 year. However, the percentage decreases as the number of years post-operation increases.

The majority of the patients are on fewer medications than they were pre-operatively. This is consistent for each year. The mean number of pre-operative medication was 2.7 and the number of medication post-operation at 1 year, 2 years, 3 years and 5 years were 1.8, 1.7, 1.8 and 1.8, respectively; this is shown in Table 7.

Table 7. Number of medications before and after BGI surgery

Number of medications	Mean ± SD (range)
Pre-operative	2.7 ± 1.2 (0-5)
Post-operative (1 year)	1.8 ± 1.4 (0-4)
Post-operative (2 years)	1.7 ± 1.4 (0-4)
Post-operative (3 years)	1.8 ± 1.5 (0-4)
Post-operative (5 years)	1.8 ± 1.5 (0-4)

Complications

The most common intra-operative complication in the surgery was bleeding (eight patients), the most common early post-operative complication was hyphema (three patients) and the most common late complication was bullous keratopathy. The post-operative complications are listed in Table 8, grouped into early and late complications.

Table 8. Early and late post-operative complications from BGI surgery

Early complications	
Hyphema	3
Choroidal detachment	2
Endophthalmitis	1
Tube blockage	1
Late complications	
Bullous keratopathy	3
Tube erosion	1
Tube blockage	1
Cystoid macular oedema	1

Discussion

This study has shown that the intermediate- to long-term results of the BGI in Asian population is satisfactory in the majority of the cases. There was a significant decrease in IOP at each follow-up visit at 1, 2, 3 and 5 years. These results are promising because of failure of medical management and poorer success of trabeculectomy augmented with antimetabolite.

There was improvement of VA in many patients after 1 year. However, the percentage decreases as the number of years post-operation increases. This suggests that the BGI can improve VA, but this improvement isn't in the long term. However, many of the patients would have lost visual potential and have continued deterioration because of the severity of their glaucoma at presentation. There were numerous other causes of further deterioration of vision other than from the glaucoma after 1 year, but these were not analysed. Most commonly patients developed cataracts, or cystoid macula oedema or have progression of their diabetic retinopathy

Generally, the incidence of post-operative complications were low. This exceeded expectations compared to previous reports. In total, 184 eyes (93.4%) did not have any post-operative complications with the BGI surgery. The most common intra-operative complications in the surgery was bleeding, in 8 cases out of 197 eyes (4.1%), most of which are from patients with neovascular glaucoma. The most common early complication was hyphema (three eyes), which resolved spontaneously after corticosteroid eye drops in 1 to 2 weeks. These cases were in those with pre-existing neovascularization and post-traumatic cases. Hyphema was prevented by slow decompression of eye during surgery, tamponade with viscoelastics during and at the end of surgery.

There was a low rate of choroidal detachment (two eyes) and suprachoroidal haemorrhage (none). In the two cases of choroidal detachment, they were due to post-operative hypotony and this has a higher incidence in previously vitrectomized eyes. Precautionary measures were taken to prevent early post-operative hypotony by ligation of tube, and instillation of viscoelastic in anterior chamber intra-operatively. One eye was treated conservatively with cycloplegic drops and resolved spontaneously, and in the other one, the anterior chamber was reformed with viscoelastic injection. None required surgical drainage.

There was one case of endophthalmitis where this patient had malignant glaucoma post-operatively, had core vitrectomy, then developed endophthalmitis, but resolved with oral and intra-vitreal antibiotics. Strict precautions were taken in all cases to prevent this complication such as good diabetic control, strictly aseptic surgical technique and intracameral and post-operative topical and oral antibiotics were routinely given.

Another complication was tube blockage; there were one case each of tube blockage in the early and late stage. Common causes are blockage due to blood, vitreous, iris or silicone oil. In both cases, the blockage was due to vitreous and had YAG laser done to clear blockage. Unlike previous series, there were no complications of wound dehiscence or flat anterior chamber; these were avoided with meticulous surgical technique.

A common late complication in this study was bullous keratopathy (three eyes). These patients had previous multiple intraocular surgeries. Precautions to prevent these complications were proper surgical technique, protection of corneal endothelium with viscoelastics and proper placement of tube away from cornea. Those with this complication were treated with steroid drops and hypertonic saline and referred to corneal surgeon for further management such as corneal transplant. One eye had cystoid macula oedema and resolved after treatment with topical non-steroidal anti-inflammatory drugs eye drops (nepafenac). Lastly, tube erosion (one eye) was managed successfully with surgical revision of wound with sclera and conjunctival graft.

One of the reasons for the lower rate of complications and longer-term success could be attributed to the surgical technique used in this study, which is slightly different from others. Mitomcyin C was routinely used in most cases, 0.2 mg/ml soaked in Weck-Cell sponge and placed between Tenon's capsule and sclera for 3 minutes and washed away by copious amount of balance salt solution. This would prevent future fibrosis and encapsulation over the plate. The number of Sherwood slits was more than the recommended, but it was done based on the surgeon's experience and the amount of viscoelastic gel left in the anterior chamber, thus preventing major immediate post-operative complications.

Comparing this study's success rate with other studies, reduction in IOP at 2 years was 50.7%, which is comparable to other studies at 2 years. This is similar to BGI in a study by Krishna *et al.* (56%), Ahmed implants (51%), double-plate Molteno implants (46-53%). This is higher than that reported with single-plate Molteno implants (25%) but lower than that reported with Krupin devices (64%).[2,6]

BGI has a bigger but flatter plate compared to other devices but is non-valved. Because of its bigger surface area, it potentially will have higher long-term rate of success, although there is not a lot in the literature about long-term outcomes. It is more difficult to implant compared to the other GDDs like Ahmed, because it is a bigger plate and is non-valved, it needed measures to prevent initial hypotony, such as tube ligation and stenting and Sherwood slits.[3,7] Initial studies shows that the success increases with the size of the plate, but up to about 500 mm^2. There are three sizes available, 250 mm^2 for young children, 500 mm^2 plate is too big and difficult to implant. The choice of 350 mm^2 was because of surgeon preference.

The Ahmed and Baerveldt (ABC) comparison study showed that with the BGI, success rates were higher and patients achieved both a statistically significant lower IOP ($p = 0.015$) and a trend toward statistical significance ($p = 0.28$) for reduced need for glaucoma medication compared to the Ahmed implant.[8] Ahmed vs Baerveldt (AVB) study showed that both devices were effective in reducing IOP and glaucoma medications. The Baerveldt group had a lower failure rate and required fewer medications than the Ahmed group after 3 years, but it experienced more hypotony-related vision-threatening complications.[9]

The results of the Tube versus Trabeculectomy study showed that patients with medically uncontrolled glaucoma who had previous cataract extraction with intraocular lens implantation and/or failed filtering surgery who were treated with tube shunt surgery were more likely to maintain IOP control and avoid persistent hypotony, loss of light perception vision or re-operation for glaucoma in comparison to those who underwent trabeculectomy with MMC.[1,10]

This study shows encouraging results of long-term effects of BGI on the IOP. The mean IOP at 3 and 5 years were 15.0 and 15.5, a reduction of 48.6% and 46.9% respectively, compared to pre-operation IOP. This shows that the IOP remains low

even in the long term. Overall success is excellent with only 3% failures. Of the failures, two eyes (1%) had no perception to light and four eyes (2%) had IOP levels more than 21 mmHg. Of those eyes, three eyes had subsequent second glaucoma implant surgeries with BGI. One eye (0.5%) subsequently had transscleral cyclophotocoagulation. None required bleb revision or needling.

With regard to the long-term success of BGI, some may last till the patient's lifetime, although over time, encapsulation of fibrous tissue over the plate causes increased resistance to flow. This study shows encouraging longer-term results in terms of IOP.

MMC augmented trabeculectomy is reported to be less successful than GDD. Studies regarding cyclophotocoagulation (TCP) show promise but potentially has more complications such as phthisis and is reserved for end-stage cases such as those with painful blind eyes and poor prognosis for vision. In this study, the decision to implant BGI was made for refractory glaucoma, where trabeculectomy will likely fail but patient still has visual potential. Those with no visual potential, transscleral cyclophotocoagulation (cyclodestructive procedure) was advised.

There is difficulty in comparison of intermediate-term and long-term follow-up studies because of lack of uniform success criteria, exclusion of high-risk patients and inclusion of patients with short-term follow-up. Our study is unique in that it attempts to address these concerns by including patients up to 5 years of follow-up, and including all types of pre-operative diagnoses to ascertain true intermediate- to long-term follow-up results. Similar to other studies, there is difficulty achieving long-term follow-up because many patients returned to their referring ophthalmologist for long-term follow-up. The limitations of this non-randomized retrospective with variable follow-up is that the data on optic nerve and visual field progression was difficult to obtain It was also unique that it was a large series of Asian patients which is valuable. The good intermediate- to long-term outcomes of BGIs in Asian eyes are encouraging for those with complicated and refractory glaucoma. The BGI appears to be an effective means of lowering IOP in patients with complicated glaucoma in Asian eyes.

The collection of data for this study was in 2015, and it will be good to know the 10-years outcome of some of those patients who had their BGI in 2007. These results will be published in the future.

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Intercellular adhesive molecule-1 (ICAM-1) in proliferative diabetic retinopathy

Andi A. Victor[1], Tjahjono D. Gondhowiardjo[1], Rahayuningsih Dharma[2], Sri W. A. Jusman[3], Vivi R. Yandri[4], Ressa Yuneta[4], Rizky E. P. Yuriza[4]

[1]Department of Ophthalmology, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia; [2]Department of Clinical Pathology, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia; [3]Department of Biochemistry and Molecular Biology, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia; [4]Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia

Abstract

Purpose: *To determine the level of intercellular adhesion molecule-1 (ICAM-1) in vitreous fluid of patients with proliferative diabetic retinopathy (PDR) and its affecting factors including HbA1c level, duration of diabetes mellitus (DM) and insulin usage.*

Methods: *A cross-sectional study was conducted in Cipto Mangunkusumo National General Central Hospital, Jakarta, Indonesia from June 2015 to August 2016. Thirty-three consecutive vitreous samples harvested from PDR patients underwent vitrectomy. The level of vitreous ICAM-1 was determined by enzyme-linked immunosorbent assay.*

Results: *Based on the glycemic status, vitreous ICAM-1 level in the uncontrolled glycemic group (21.61 ng/ml) was lower than controlled glycemic group (24.20 ng/ml). Patients with DM for more than 10 years had higher level of vitreous ICAM-1 (26.30 ng/ml). Vitreous ICAM-1 level in DM patients with insulin was higher than those without insulin (27.07 ng/ml vs. 24.17 ng/ml). There was no statistically significant difference between vitreous ICAM-1 levels among all groups ($p > 0.05$).*

Conclusion: *The concentration of vitreous ICAM-1 may not be influenced by glucose control and conventional insulin therapy.*

Keywords: *diabetic retinopathy, insulin, intercellular adhesion molecule-1, type 2 diabetes mellitus*

Introduction

Diabetic retinopathy (DR) is a serious micro-vascular complication of type 2 diabetes mellitus (T2DM) resulting in visual impairment and blindness, affecting those in productive age.[1,2] The advanced stage of DR, proliferative diabetic retinopathy (PDR), is characterized by neovascularization and epiretinal outgrowth of

Correspondence: Andi A. Victor, MD, PhD, Vitreoretinal Division, Department of Ophthalmology, Faculty of Medicine, University of Indonesia, Cipto Mangunkusumo Hospital-Kirana, Jl. Kimia no. 8, Menteng, Central Jakarta, DKI Jakarta, Indonesia 10320
E-mail: arvimadao@yahoo.com

fibrovascular membranes (FVMs) in the retina. This fibrovascular tissue could progress into tractional retinal detachment and vitreous haemorrhage leading to visual loss.[3,4]

DR is the most common retinal vascular disorder found in Cipto Mangunkusumo General Hospital (CMGH), Indonesia. Based on preliminary study of 3,988 medical records, 60% of DR patients who were hospitalized from 2004 to 2009 suffered from non-PDR, while the remaining suffered from PDR. In 2010 to 2012, the percentage of PDR patients increased to 47.9%, suggesting increased number of PDR patients over the years.

Despite the effort of early detection and tight glucose control in T2DM patients, the number of PDR cases is still rising. In addition, advances in treatment of PDR remains constant, adding more burdens to the problem.

Recent studies have found novel factors involved in the progression of PDR, one of which is intercelullar adhesion molecule-1 (ICAM-1).[5] ICAM-1 is an intercellular adhesion molecular whose production is triggered by vascular endothelial growth factor (VEGF) and plays vital role in the development of retinal leukostasis in DR patients.[6,7]

Due to the rising magnitude of DR and its consequences, understanding the pathophysiology of PDR is pivotal, especially of ICAM-1 and its role in progression of PDR and complications. Therefore, we aimed to investigate the concentration ICAM-1 in PDR patients related to glycemic status, the duration of diabetes and the use of hypoglycemic agents.

Materials and methods

Study design

A cross-sectional study was conducted from June 2015 to August 2016; T2DM patients with PDR were considered for enrollment into the study, held in Vitreoretinal Division, Department of Ophthalmology, Faculty of Medicine Universitas Indonesia (FMUI)—CMGH, Jakarta, Indonesia. The study has received ethical clearance from the Ethic Research Committee, FMUI (350/UN2.F1/ETIK/IV/2016). Written informed consent was obtained from all patients prior to their enrollment in this study.

In this study, all eligible participants underwent systemic evaluation, which included duration of DM, measurement of blood pressure and level of serum HbA1c.

Inclusion and exclusion criteria

Inclusion criteria were T2DM patients who have been diagnosed with PDR and were planned for pars plana vitrectomy (PPV). Patients who were recruited must have no prior history of intravitreal bevacizumab or laser photocoagulation.

Patients who suffered from uncontrolled hypertension (systolic > 180 mmHg or diastolic > 110 mmHg), coagulation disorder or using anticoagulant within the last 1-week, kidney failure (hemodialysis patients), history of stroke, congestive heart failure and collagen disorder (rheumatoid arthritis, systemic lupus erythematous or systemic sclerosis) were excluded from the study. In addition, patients with severe vitreous haemorrhage, who were unable to be examined for their fundus and optical coherence tomography, were excluded.

Patients' enrollment

Consecutive vitreous sampling was done and 33 samples were recruited. Data regarding duration of T2DM, level of HbA1c, insulin use and mean of vitreous ICAM-1 level were obtained.

Vitreous and plasma samples

Undiluted vitreous fluid samples (0.5-1.0 ml) were harvested from 33 patients with PDR by PPV. Vitreous samples were collected with 1 ml syringe and transferred into sterile tubes and put into a container filled with blue ice/dry ice. Afterwards, samples were frozen rapidly at –80°C until assayed. Blood samples were also collected into vacuum tubes, and directly sent to the laboratory for HbA1c examination.

Pars plana vitrectomy

PPV was performed using the standard three-port incisions in combination with dissection and removal of the vitreous haemorrhage and FVM. Endolaser retinal photocoagulation was done in each eye with the power of 300 to 500 mW, duration of 200 to 300 ms, interval of 200 to 300 ms and number of laser shots 300 to 600. Silicone oil was used as tamponade in all participants.

Measurement of ICAM-1

ICAM-1 level was measured from the vitreous samples by the Department of Clinical Pathology, FMUI-CMGH, Jakarta, Indonesia. Evaluation of ICAM-1 in vitreous was performed by using human ICAM-1/CD54 non–allele-specific Quantikine kit (DCIM00; sensitivity test 0.053 ng/ml; intra-assay coefficient variation 4.04%; inter-assay coefficient variation 6.28%) for enzyme-linked immunosorbent assay. The standard solution (50 µl for ICAM-1) and the sample (50 µl for ICAM-1) were put in to the wells of a well plate coated with the relevant monoclonal antibody. The assay procedure was done according to the manufacture's instruction (R&D systems). The intra-assay precision and the amount of the product was then quantitated as nanogram per milliliter (ng/ml).

Statistical analysis

All statistical analyses were performed with Microsoft Excel 2007 and Statistical Package for Social Sciences Software for Windows, version 21.0 (SPSS Inc., Chicago, IL). P-value of less than 0.05 was considered significant.

Results

Thirty-three eligible PDR patients were included in this study. The characteristics of the subjects were described in Table 1. Participants who had uncontrolled glycemic status tend to have lower vitreous ICAM-1 compared to those with controlled glycemic status. However, the difference was not found to be statistically significant (p = 0.65, Table 2).

Participants who had T2DM for more than 10 years also had higher level of vitreous ICAM-1 than participants with less than 10 years duration of T2DM.

Table 1. Main clinical features of diabetic patients with PDR in the study

Characteristic	Control (n = 33)
Age (range), years	51 (26-66)
Sex (%)	
Male	14 (42.4%)
Female	19 (57.6%)
Duration of diabetes (range), years	
≤10 years (n = 21)	2.5 (1-10)
>10 years (n = 12)	17.5 (11-30)
HbA1c (range), %	
≤7 (n = 6)	6.5 (5.3-7)
>7 (n = 28)	8.9 (7.2-13.5)
Use of hypoglycemic agent (%)	
With insulin	12 (36.4%)
Without insulin	21 (63.6%)

Table 2. The influence of HbA1c level in the concentration of vitreous ICAM-1 in PDR patients

Level	Glycemic control (HbA1c)		p
	Controlled (≤7 g/dl)	Uncontrolled (>7 g/dl)	
Mean ICAM-1 (ng/ml) ± SD	24.20 ± 13.05	21.61 ± 13.29	0.650[a]

[a] *p-value* by unpaired T-Test
SD, standard deviation

Nevertheless, there was no statistically significant difference between both groups (p = 0.64, Table 3).

We also found that participants with insulin had higher level of vitreous ICAM-1 compared to those without insulin. However, there was no statistically significant difference between groups (p = 0.55, Table 4).

Table 3. The influence of diabetes duration in the concentration of vitreous ICAM-1 in PDR patients

Level	Duration of diabetes		p
	≤10 years	>10 years	
Mean ICAM-1 (ng/ml) ± SD	24.17 ± 14.85	26.30 ± 10.42	0.643[a]

[a]*p-value* by unpaired T-Test
SD, standard deviation

Table 4. The influence of insulin therapy in the concentration of vitreous ICAM-1 in PDR patients

Level	Use of hypoglycemic agents		p
	With insulin	Without insulin	
Mean ICAM-1 (ng/ml) ± SD	27.07 ± 10.95	24.17 ± 13.88	0.551[a]

[a]*p-value* by unpaired T-Test
SD, standard deviation

Discussion

Hyperglycemia leads to the progression of DR by increasing intraocular inflammatory activity, inducing retinal endothelial dysfunction and damaging blood–retinal barrier (BRB).[8] The role of inflammatory factors and cytokines in the progression of DR, including ICAM-1, has been researched in many studies.[8] The aim of this study was to determine the level of vitreous ICAM-1 in PDR patients and identify ICAM-1–affecting factors, including HbA1c level, duration of T2DM and use of insulin. A total of 33 eligible subjects with diagnosis of PDR were collected. In this study, 57.6% of subjects were female and 42.4% were male.

One factor that can influence the concentration of ICAM-1 is the duration of T2DM. Ghonaim and El-Edel[9] reported an increase of the serum ICAM-1 level in patients who suffered from T2DM for more than 10 years. They believed that the duration of T2DM would induce micro-vascular complication that provoked endothelial expression of adhesion molecules. We also found an increase of

vitreous ICAM-1 level in participants who had suffered from T2DM for more than 10 years. Nevertheless, this result was not statistically significant. As the duration of diagnosis was obtained from interview, this result may include recall bias.

Several authors have reported the level of ICAM-1 in DR. Mroczek *et al.*[8] found that vitreous ICAM-1 concentration in PDR patients was higher than the control group (19.58±20.65 ng/ml and 4.12±3.14 ng/ml, respectively). In addition, other studies have been reported a significant increase of vitreous ICAM-1 in patients with diabetes compared with non-diabetic patients.[10,11] A study found that ICAM-1 in patients with active PDR was higher than in those with inactive PDR.[12] Nevertheless, Ruszkowska-Ciastek *et al.*[13] showed that there was a significant decrease of serum ICAM-1 level in uncontrolled T2DM patients (HbA1c > 6.5%) compared with well-controlled group (HbA1c < 6.5%; $p < 0.05$). Noda *et al.*[14] also showed that the level of ICAM-1 was substantially reduced in subjects with HbA1c > 10%. We found similar result with Ruszkowska-Ciastek and Noda's studies. Our study demonstrated that vitreous ICAM-1 concentration in uncontrolled T2DM (HbA1c > 7%) was lower than in participants with well-controlled T2DM. Yet, our study observed no statistical differences in ICAM-1 level between both groups ($p > 0.05$). Unfortunately, the exact nature of this phenomenon is still not yet fully understood.

The BRB consists of an outer component, the retinal pigment epithelium and an inner component, the retinal vascular endothelium.[15] ICAM-1 is believed to be produced in the retinal pigment epithelium by the influence of VEGF expression.[16] In hyperglycemic condition, the increase of ICAM-1 level mediates leukocytes adhesion to the retinal vessels influencing the vascular permeability, leading to retinal endothelial cell injury and death. This circumstance may lead to BRB breakdown and sub-endothelial basement membrane stiffness.[17] Yet, after a certain period of time, we assumed that ICAM-1 level might decrease because the entire BRB layer and vascular basement membrane has already broken down. This might be the possible reason of our findings in this study. Stratifying the data based on disease duration with large sample size may help.

The usage of insulin has been believed to affecting the level of ICAM-1 in DM patients. King *et al.*[18] and Jingi *et al.*[19] suggested that retinal capillary endothelium was insulin-sensitive tissue. Hirata *et al.*[20] reported that the expression of ICAM-1 increased in healthy human retinal endothelial cells incubated with 100 μU/ml insulin therapy for 48 hours. They demonstrated that acute-intensive insulin therapy induced the production of cell adhesion molecules on retinal endothelium, including ICAM-1. In this study, vitreous ICAM-1 level in T2DM participants with insulin was higher than T2DM patients with hypoglycemic drugs, yet there was no statistically significant difference between both the groups. T2DM participants from the insulin group in this study were treated by conventional insulin

therapy, whereby they regularly got insulin injections of a mixture of rapid and long-acting insulin. Thus, we assumed that conventional insulin therapy might not have any direct effect in increasing the level of ICAM-1 concentration in vitreous.

Conclusion

ICAM-1 has been known to have a correlation with the progression of DR, by up-regulating VEGF and inducing retinal vascular endothelial inflammation. We concluded that conventional insulin therapy might not have direct effect on the vitreous ICAM-1 concentration. On the other hand, uncontrolled T2DM remained a controversial factor in influencing the level of ICAM-1. Limitation of our study includes presence of blood in the vitreous. Although those with severe haemorrhage were excluded, some may still have some amount of blood in the vitreous. Hence, this might affect the results. In addition, other control parameters, such as western blot, were not done. This might influence the sensitivity of the procedure to determine the result. We recommend further investigation could be conducted in order to understand the pathogenic mechanism of retinal micro-vascular abnormality in diabetic patients. Moreover, utilizing more than one method for detecting ICAM-1 may be essential for increasing the accuracy of the result.

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Avoiding BAK in postoperative eye drops reduces the need for subconjunctival 5-FU injections post-trabeculectomy

Keith Ong[1,2,3,4], **Leonard Ong**[4,5,6]

[1]Department of Ophthalmology, Northern Clinical School, University of Sydney, Sydney, Australia; [2]Department of Ophthalmology, Royal North Shore Hospital, Sydney, Australia; [3]Department of Ophthalmology, Sydney Adventist Hospital, Sydney, Australia; [4]Department of Ophthalmology, Chatswood Private Hospital, Sydney Australia; [5]Ophthalmology Clinic, Macquarie University Hospital, Sydney, Australia; [6]Department of Clinical Medicine, Faculty of Medicine and Health Sciences, Macquarie University, Sydney, Australia

Abstract

Purpose: *Subconjunctival fibrosis is one of the main causes of failure of glaucoma filtration surgery. It can result in absence of a filtration bleb, a small scarred bleb, or a cystic bleb. 5-Fluorouracil (5-FU), mitomycin C (MMC), and topical steroids have been used to suppress subconjunctival fibrosis.*

Method: *A study was done analyzing the number of postoperative subconjunctival 5-FU injections for trabeculectomy on pseudophakic eyes prior to and following the change to a BAK-free regimen. The cohort consisted of 16 consecutive cases undergoing primary trabeculectomy without intraoperative MMC or 5-FU. The trabeculectomy surgery included a groove sclerectomy procedure.*

Group A were 8 eyes of patients who had the author's standard Chlorsig, Maxidex, and Prednefrin Forte eye drops tds. Group B were 8 eyes who had Chlorsig-dexamethasone and Optive-dexamethasone tds eye drops postoperatively.

Results: *Group B (BAK-free) patients required fewer postoperative 5-FU subconjunctival injections (average: 2.9, range: 1-5 injections) compared to Group A (BAK) patients (average: 7.3, range: 4-18 injections). This difference was statistically significant (P = 0.02, unpaired t-test).*

All patients had functioning blebs and did not require glaucoma medications to maintain target intraocular pressure. The Group B (BAK-free) patients had more diffuse blebs than the Group A (BAK) patients.

Conclusion: *The results demonstrated that when BAK was eliminated from postoperative eye drops in trabeculectomy, the number of postoperative 5-FU injections was reduced.*

Correspondence: Dr. Keith Ong, 2 Railway Avenue, Eastwood NSW 2122, Sydney, Australia.
E-mail: keithong@optusnet.com.au

Introduction

Subconjunctival fibrosis is one of the main causes of failure in glaucoma filtration surgery. It can result in absence of a filtration bleb, a small scarred bleb, or a cystic bleb. 5-Fluorouracil (5-FU), mitomycin C (MMC) and topical steroids have been used to suppress subconjunctival fibrosis.

In patients with meibomian gland dysfunction, or inflammation related to long -term use of glaucoma eye drops containing benzalkonium chloride (BAK), subconjunctival fibrosis is more prevalent.[1]

Background

The author had a trabeculectomy patient who was allergic to BAK. All the commonly used postoperative steroid eye drops such as Maxidex (Alcon), Prednefrin Forte (Allergan), FML (Allergan), Flucon (Alcon), Flarex (Alcon) contain BAK, and hence, could not be used. Siguent Hycor 1% (Aspen Pharma) eye ointment was used as it did not contain BAK preservative. As this would not give sufficient anti-inflammatory effect, two vials of dexamethasone for injection (Mylan) (1 ml of 4 mg/ml dexamethasone) was added to Chlorsig (Aspen Pharma) eye drops (10 ml) and also Optive eye drops (15 ml). Chlorsig contain phenyl mercuric acetate preservative and Optive (Allergan) contain purite preservative. Both of these dexamethasone BAK-free combination drops were used postoperatively tds. As this regimen resulted in a favorable functioning bleb requiring only five postoperative 5-FU injections, it was decided to use this BAK-free regimen for all patients from September 2018.

Mild BAK allergy and toxicity usually does not cause much conjunctival inflammation because the steroid eye drops mask the inflammatory reaction.

Method

A retrospective audit study was done analyzing the number of postoperative subconjunctival 5-FU injections for trabeculectomy on pseudophakic eyes prior to and following the change to a BAK-free regimen. The consecutive cases analyzed were for primary trabeculectomy on pseudophakic eyes and did not have intraoperative MMC or 5-FU. The trabeculectomy surgery included a groove sclerectomy procedure.[2] Patients having combined cataract phacoemulsification and trabeculectomy and revision trabeculectomy were excluded.

Results

The cohort (Table 1) consisted of 16 consecutive eyes which had trabeculectomy, were pseudophakic, and of Chinese ethnicity. Group A comprised 8 eyes of patients with average age 70.4 years with range of 64 to 83 years of age who

Table 1. Group comparison of postoperative 5-FU injections and age

	Group A (with BAK)		Group B (BAK-free)	
	Postoperative 5-FU	Age	Postoperative 5-FU	Age
Patient 1	7	83	5	68
Patient 2	18	65	3	93
Patient 3	4	66	2	66
Patient 4	7	67	1	81
Patient 5	4	71	4	64
Patient 6	6	80	1	64
Patient 7	5	67	5	66
Patient 8	7	64	2	79

had the author's standard Chlorsig, Maxidex, and Prednefrin Forte eye drops tds. Group B comprised 8 eyes of patients with average age 72.6 years and range from 64 to 93 years of age who had Chlorsig-dexamethasone and Optive-dexamethasone tds eye drops postoperatively.

Discussion

Group A and Group B did not differ significantly in age (P = 0.62, unpaired t-test).

Group B (BAK-free) patients required fewer postoperative 5-FU subconjunctival injections (average: 2.9, range: 1-5 injections) compared to Group A (BAK) patients (average: 7.3, range: 4-18 injections). This difference was statistically significant (P = 0.02, unpaired t-test). If the patient with the highest number of 5-FU injections is excluded from each group, since patient 2 in Group A had a much higher number compared to all patients and may have led to this statistical significance, an even more statistically significant result is obtained (2.6 in BAK-free versus 5.7 in BAK groups, P = 0.002).

All patients had functioning blebs and did not require glaucoma medications to maintain target intraocular pressure. The Group B (BAK-free) patients had a more diffuse bleb than the Group A (BAK) patients.

The results demonstrated that when BAK was eliminated from postoperative eye drops in trabeculectomy, the number of postoperative 5FU injections was reduced.

Conclusion

Changing the postoperative eye drops to exclude BAK does not pose any risk and could increase the success of all glaucoma surgery with bleb formation. It would improve the outcome of minimally invasive glaucoma surgical procedures such as the Xen implant by reducing the number of postoperative bleb needling and injections. Furthermore, avoiding BAK in glaucoma drops that have to be used following bleb surgery could increase the long-term survival of blebs.

In conclusion, this study is consistent with reduced subconjunctival fibrosis when BAK is avoided postoperatively. A practical method of preparing steroid eye drops without BAK has been described and would be useful until BAK-free steroid eye drops are easily available and affordable.

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