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EDITORIAL BROAD

Vol. 14 Issue 2 **July-December 2019**

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Data and knowledge to empower healthcare in South East Asia and beyond

To our readers,

On behalf of the editorial team, I would like to welcome you to EyeSEA journal. I am very pleased to announce the launch of this new issue. Our continued growth of authorship and readership has been reflected in the great variety of articles compiled in this current release. This success would not be possible without dedication and encouragement from our authors, reviewers, and editorial team.

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Warmest regards,

Associate Professor Sakchai Vongkittirux, MD
Head of Thammasat Eye Center,
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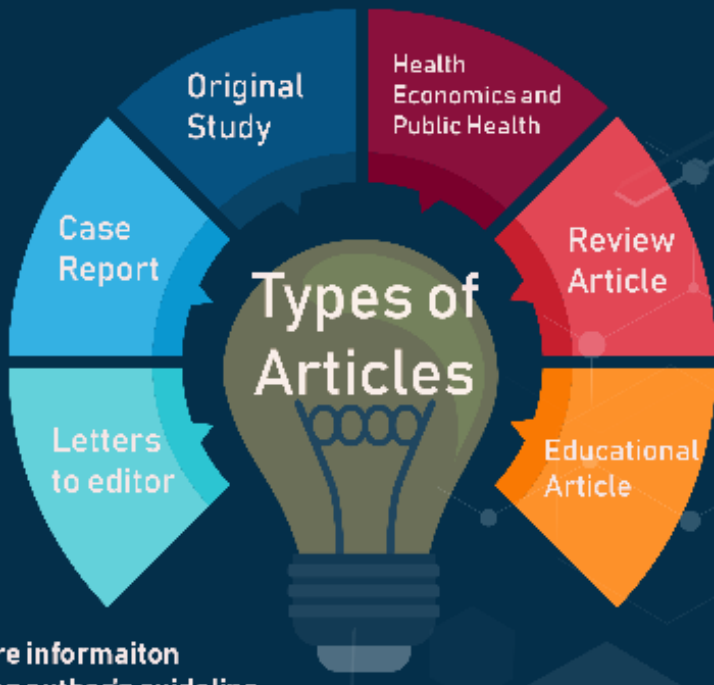

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Aims and Scope and Publication Policy

Aims and Scope

Eye South East Asia (EyeSEA) strives to promote the dissemination of regionally relevant academic publications and discourse in the field of Ophthalmology. The South East Asian population has a unique spectrum of eye diseases due to pathophysiologic, geographic, socioeconomic and cultural contexts – although often underrepresented in literature. EyeSEA supports the growing number of ophthalmic healthcare professionals in the region seeking to produce and disseminate academic publications, developing robust clinical methodology and quality of original publications in Ophthalmology from South East Asia to the world.

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Your abstract must contain content for the following headings:

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3.Methods (Leave this section blank for case report)
4.Results ("Case report", summarise the case for case report, "Case series" summarise all cases for case series)
5.Conclusion
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Methods

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-The results of the analysis of the primary objectives, mentioning statistical method, expressed in words and numbers along with *P* in parenthesis

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-Important negative findings, if any should also be presented: that is, findings that fail to support the authors' hypothesis

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Conclusion

-The primary take-home message

-The additional findings of importance

-The perspective

Our guidelines are based on the following reference: Andrade C. How to write a good abstract for a scientific paper or conference presentation. Indian Journal of Psychiatry. 2011;53 (2):172.

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- Results
- Discussion
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Ocular bungee cord trauma: clinical characteristics and treatment outcomes

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Background: The use of the bungee cord is still common in our society, resulting in ocular trauma related to its use, that is often times very complicated. Literature regarding this form of trauma is scarce, mostly case reports; therefore a more detailed study of bungee cord ocular trauma is beneficial.
Objectives: To describe clinical features and treatment outcomes of ocular trauma associated with bungee cord injuries.
Methods: Prospective case series. One hundred cases of bungee cord-associated ocular trauma who underwent in-patient and out-patient treatment at Cosmetic – Neuro-Ophthalmology Department, Ho Chi Minh City Eye hospital from March 2018 to December 2018 were enrolled in this study. Baseline visual acuity and intraocular pressure, anterior segment, posterior segment and periorbital injuries and surgical intervention were recorded. Follow-up period was 6 months for all the patients.
Results: Fourty-four% of patients had hand movement and light perception visual acuity. The most common anterior, posterior and periorbital injuries were hyphema (79%), vitreous hemorrhage (40%) and eyelid edema/ecchymosis (61%). Fifty-one percent underwent surgical intervention, with the most common surgery being corneal-scleral reconstruction (30%). Forty-five percent had visual acuity improved after treatment, while 30% of patients remained counting finger to no light perception.
Conclusion: Bungee cord may cause a varied spectrum of injuries, with low baseline visual acuity and poor prognosis. A modification in the design of these cords, as well as appropriate printed warnings to the users regarding the potential for severe ocular trauma and preventive strategy, is therefore necessary.
Conflicts of interest: The authors report no conflicts of interest.
Keywords: bungee cord, ocular trauma, clinical characteristics, treatment outcomes.
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Introduction

Ocular trauma resulting from bungee cords, elastic cords with metallic J-shape hooks at both ends (Figure 1), have become increasingly prevalent. With low price and ease of acquisition, bungee cords

are usually used in occupational and recreational events. When recoiled, the elastic cord generates an immense power which enables the metallic hook to injure the eye. The design of the cord enables it to cause both open and closed globe injuries when one of the hooks are not appropriately secured or when the hook is straightened by the force of the loads secured.

A few studies regarding this type of trauma have been carried out[1-9], mostly being case series with participants of less than 30; the largest study had 67 participants[1]. In those studies, the authors agreed that most patients were male, and that a considerable number of patients required surgery. Furthermore, these cords should be modified with a warning paper about the risk of ocular trauma paired with it.

Figure 1: The design of a bungee cord

Due to the increasing number of patients and few studies about this subject, we conducted this study to describe clinical manifestations and treatment outcomes of bungee cord associated ocular trauma, as well as to support previous authors in the calling for a structure modification of this cord.

Materials and methods

This study, a prospective case series, was carried out in Ho Chi Minh City Eye Hospital from March 2018 to December 2018. Participants were all patients whose eyes were injured by a bungee cord with 2 J-shaped hooks, treated in outpatient unit or hospitalized in the cosmetic – neuro-ophthalmology department of the hospital in the above period of time. Patients who had previous history of vision-affected eye diseases, did not complete 6-month follow up or did not agree to participate were excluded from this study.

For data collection, we recorded patients age, sex, occupation, setting of trauma event, duration until admission to hospital, baseline visual acuity (VA) – classified based on visual acuity grading of WHO - and intraocular pressure (IOP), periocular, anterior segment and posterior segment manifestations, operations performed, hospitalized duration. We also recorded VA and IOP of all the patients until 6-month follow-up.

Results

From March 2018 to December 2018, 100 patients with bungee cord ocular trauma were studied. Etiological characteristics of the patients were summarized in Table 1. In this study, most of the patients were male, either workers or farmers of working age. Most patients (71%) suffered the trauma when securing the cord, with the main reason being the cord was let cord slip (85%). Ninety-seven percent had not used protective glasses, and most patients (84%) were admitted to hospital immediately after the trauma.

Baseline VA, IOP and clinical manifestations of the patients were summarized in Table 2. Most patients (61%) had baseline VA being counting fingers (CF), hand-movement (HM) or light perception (LP), 7% had no light perception (NLP); 53% of patients had baseline VA outside of normal limits. The most common periorbital injury was eyelid edema and/or ecchymosis (61%). Three most common anterior segment injuries were hyphema (79%), angle recession (51%) and lens dislocation (40%).Thirty-three percent had corneal-scleral laceration, in whom 30/33 cases had penetrating lacerations. The most common posterior segment injury was

vitreous hemorrhage (40%), following by commotio retinae (28%) and retinal hemorrhage (23%).

Table 1: Etiological characteristics of the patients

Etiological characteristics	N (%)
Age	
<18	1 (1)
18-60	96 (96)
>60	3 (3)
Gender	
Male	79 (79)
Female	21 (21)
Location	
Ho Chi Minh City	19 (19)
Others	81 (81)
Career	
Students	1 (1)
Worker	83 (83)
Housework	5 (5)
In-office work	7 (7)
Retired	4 (4)
Initiating incident	
Cord securing	71 (71)
Cord release	29 (29)
Cause	
Cord slipping	85 (85)
Cord broken	9 (9)
Others	6 (6)
Secured glasses equipment	
With	3 (3)
Without	97 (97)
Duration until admission	
Immediately	84 (84)
1-3 days	12 (12)
>3 days	4 (4)

Treatment characteristics were summarized in Table 3. Every patient needed medical treatment and 51% needed to undergo surgery, with the most common procedure being corneal-scleral reconstruction (30%). Seventy-two percent of patients needed to be hospitalized, most of them (59%) were hospitalized for 4-7 days.

Table 2: Baseline VA, IOP and clinical manifestations of patients

Clinical characteristics	N (%)
VA	
≥14/20	5 (5)
8/20-12/20	9 (9)
2/20-6/20	18 (18)
CF	17 (17)
HM-LP	44 (44)
NLP	7 (7)
IOP	
High (≥21 mmHg)	15 (15)
Normal (17-20 mmHg)	47 (47)
Low (≤16 mmHg)	38 (38)
Periocular injury	
Lid edema/ecchymosis	61 (61)
Lid laceration	11 (11)
Conjunctival laceration	22 (22)
Medial rectus muscle tear	1 (1)
Anterior segment injury	
Corneal abrasion	8 (8)
Hyphema	79 (79)
Angle recession	51 (51)
Iris sphincter tear	13 (13)
Lens dislocation	40 (40)
Corneal-scleral laceration	33 (33)
Posterior segment injury	
Commotion retinae	28 (28)
Vitreous hemorrhage	40 (40)
Retinal hemorrhage	23 (23)
Retinal tear	2 (2)

Patients VA and IOP in follow up examinations were summarized in Figure 2A and Figure 2B. At 6-month follow up, 45% of patients had improved VA; however, thirty percent remained CF to NLP. Twenty-one percent of patients had high IOP at 6-month follow up, all patients responded well with IOP-lowering drugs.

Table 3: Treatment characteristics of the patients

Treatment	N (%)
Surgical intervention	
Lid repair	2 (2)
Conjuntival reconstruction	7 (7)
Corneal-scleral reconstruction	30 (30)
Anterior chamber blood removal	15 (15)
Lensectomy	9 (9)
Vitrectomy	7 (7)
Muscle reconstruction	1 (1)
Hospitalized duration	
0 day	28 (28)
1-3 days	9 (9)
4-7 days	59 (59)
>7 days	4 (4)

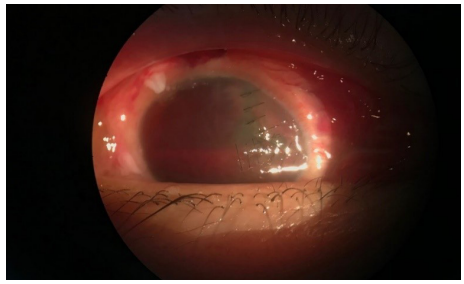


Figure 3: A bungee cord ocular trauma patient with penetrating corneal laceration (reconstructed), hyphema and vitreous hemorrhage (B-scan ultrasound)

Discussion

Similar to previous authors, our study demonstrated that bungee cord use could cause severe ocular trauma (Figure 3). Seventy-two percent of patients being hospitalized, 51% undergoing surgery and CF to NLP visual acuity accounted for two-thirds of patients at baseline and one-third of patients at 6-month follow up, confirmed the danger of trauma by this cord. Although blunt trauma accounted for most cases, 30% of patients suffered penetrating injuries with severe reduction of visual acuity. Most patients were male (79%) and of working age (96%), many of them may be the main working individual in family. Bungee cord associated ocular trauma may cause these patients irreversible vision loss, which is a considerable impact for the families and society. Barely any of the patients were aware of the dangers of working with bungee cords when only 3% used protective plastic glasses while securing their belongings. On the other hand, all the

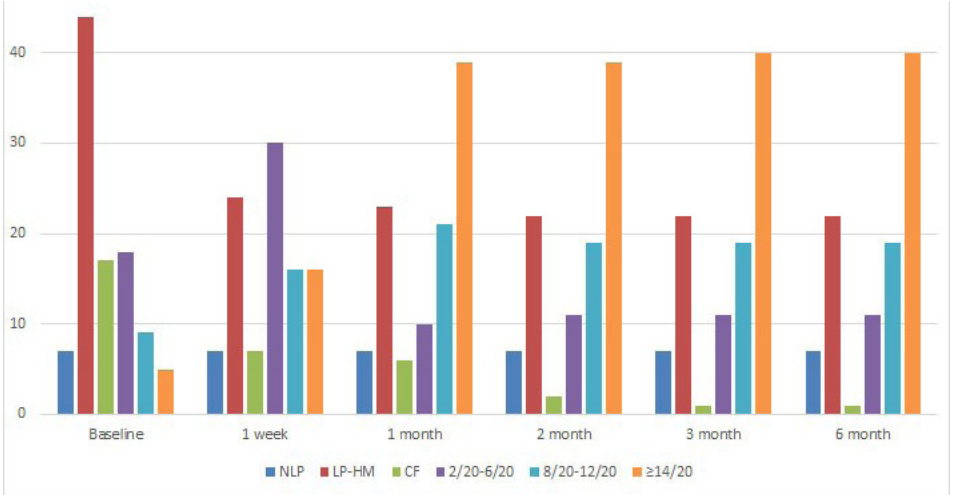
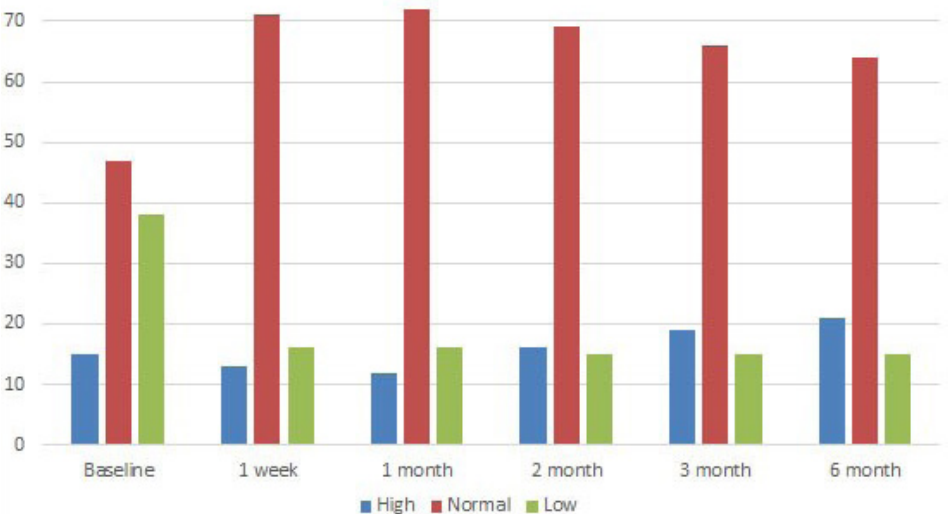


Figure 2A: Patients VA at follow-up examinations

Figure 2B: Patients IOP at follow-up examinations



patients used protective glasses admitted to hospital with penetrating corneal – scleral laceration. Our study group considered if the broken pieces of the glasses caused even more severe damage to the eye.

To the best of our knowledge, this is the largest series regarding bungee cord ocular trauma up to now. Most studies, including our own, found that the majority of patients were males in working age[1-3]. Hyphema was the most common anterior segment finding. One study[3], along with ours, found that vitreous hemorrhage was the most common posterior segment finding, along with other findings such as retinal tears[5,8] and commotio retinae[1]. This difference may be the result of difficulty in examining the posterior segment in vitreous hemorrhage patients of whom the the authors used B-scan ultrasonography to look for other signs. The percentage of patients who required surgery varied from study to study[1-3]. This difference possibly comes from the decision ofwhether or not to perform surgery to remove anterior segment blood, which depends on the knowledge, experience and skill of the surgeons.

The trade and use of bungee cords is not an illegal act; moreover, the price of bungee cords is affordable and it is easy to access. Therefore, the only solution to prevent the damage of bungee cord to users is to modify its structure. As recorded above, 79% of trauma cases happened when the patients were securing the cord, and 85% of cases were because the cord slipped from its secured location. Therefore, most of trauma cases could be prevented if the S-shaped hook is modified into an O-shape with a gate flip (Figure 4). This modified structure would prevent the hook from being released unless the flip was depressed, therefore prevent most users from ocular trauma. From our

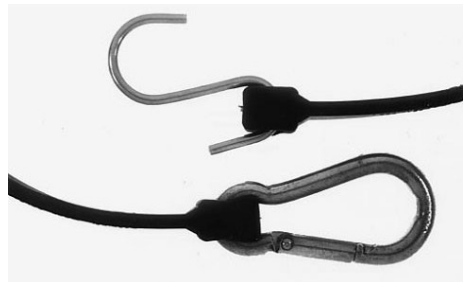


Figure 4: An example of a modified bungee cord, with S-shape hook replaced by a gate flip

study results, it is unlikely that bungee cord users are willing to use protective glasses; therefore it is reasonable that making bungee cords safer is the responsibility of the manufacturers.

Conclusion

Being the largest case series to date regarding bungee cord-associated injury, this study demonstrates that this tool may cause a varied spectrum of injuries. Among those injuries, many are serious and complicated, with low presenting visual acuity and bad prognosis. A modification in the design of these cords, as well as an appropriate printed warnings to users regarding the potential for severe ocular trauma and preventive strategy, is therefore necessary.

Acknowledgements

This study was supported by Ho Chi Minh City Eye Hospital research fund.

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A case of central retinal artery occlusion secondary to untreated barlow type D carotid cavernous fistula

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Background: To report a case of central retina artery occlusion after failed coiling in a Barrow Type D carotid cavernous fistula (CCF).
Methods: Case Report
Results: A sixty-four-year-old male with no prior history of trauma, presented with insidious onset of right eye proptosis with corkscrew vessels and bruit with increased intraocular pressure (IOP) but no blurring of vision and normal retina. Radiological examination showed Type D CCF. Cerebral coiling was performed but failed and resulted in worsening vision and intraocular pressure and noted to have central retina artery occlusion (CRAO). Secondary embolization was performed which obliterated the fistula, in which the patient recovered favorable visual function.
Conclusion: CRAO is a rare complication of cerebral coiling, in which the patient regained favorable visual function. This report describes our experience of CRAO post cerebral coiling which recovered after obliteration of the fistula by embolization.
Conflicts of interest: The authors report no conflict of interest.
Keywords: Carotid cavernous fistula, Barrow D, central retina artery occlusion, chemosis, proptosis, secondary glaucoma.
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Case history

Patient is a 64 years old Malay gentleman, with underlying hypertension and diabetes mellitus (T2DM) on medications. He first presented to the eye clinic in November 2015, with chief complain of redness of his right eye, without pain nor blurring of vision. He denies any systemic symptoms such as weight loss, joint pain, skin lesion or cough. Vision at this time was 6/6 bilaterally. Examination showed diffuse injection with red nodule at the nasal aspect of the sclera which did not blanch with vasoconstrictor. No signs of necrotizing, thinning of sclera or intraocular inflammation noted. General examination showed unremarkable findings. There was no sclera thickening on B scan and T-sign was negative. Initial diagnosis was nodular anterior scleritis with a

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differential of nodular episcleritis. He was started on topical steroid (Dexamethasone 0.1%) and was blood investigation was sent to rule out connective tissue disease. His red eye improved over the course of two weeks but the antinuclear antibody test (ANA) was positive (1:40, speckle pattern). Other tests were unremarkable. He was then referred to rheumatologist for further management.

One month later, he presented again with progressive right eye redness and swelling associated with visual acuity of 6/18 in his right eye. No history of trauma and he denied hearing any whooshing sound. On examination of the right eye, proptosis with chemosis and cock screw vessels were noted. Ocular motility was restricted in all directions of gaze. There was a difference of 9 mm on exophthalmometer measurement. The right pupil was mid dilated with evidence of relative afferent papillary defect. Intraocular pressure was 35 mmHg. The eyeball was not retropulsible and there was no bruit or thrill noted. Fundus examination showed pink optic disc both eyes with cup to disc ratio of 0.7 bilaterally. There were flamed shape hemorrhages near the disc and macula area. B scan showed flat retina with no fluid collection in the choroidal spaces. Provisional diagnosis at that time was right carotid cavernous fistula. He was started on oral acetazolamide and topical timolol/azopt/xalatan on the right eye to reduce the intraocular pressure (IOP).

An urgent CT brain/orbit revealed evidence of right eye proptosis and dilated right superior ophthalmic vein measuring 4mm in diameter. CT angiogram showed right cavernous sinus enlargement and dilated right superior ophthalmic vein (Figure 1). Cerebral angiogram showed type D carotid cavernous fistula with contralateral draining into left superior ophthalmic vein (Figure 2). Cerebral coiling was attempted but was failed due to inability to cannulate the fistula. At this point, his right eye became more proptosed (Figure 3) and his vision reduced

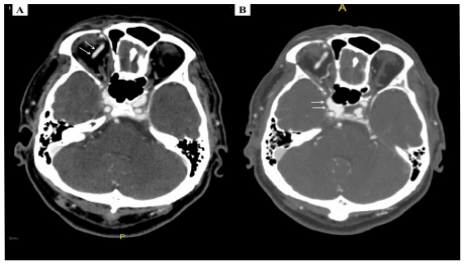

Figure 1: Computed tomography angiogram of the brain in axial view showing (A) dilated right superior ophthalmic vein and (B) enlargement of the right cavernous sinus (Source of Photo: Courtesy of Radiology Dept. Hospital of University Malaya).

to hand movement. His IOP was also not controlled (increased to 41 mmHg) despite being on 3 topical anti glaucomas. Right eye paracentesis was done to reduce the IOP and lateral canthothomy performed to help close the eyelids and protect the cornea. Fundus examination showed hazy media.

Second attempt of embolization of the fistula using liquid embolic system (PHIL 25-precipitating hydrophobic injectable liquid) was done through the external carotid artery (Figure 4). CT brain post

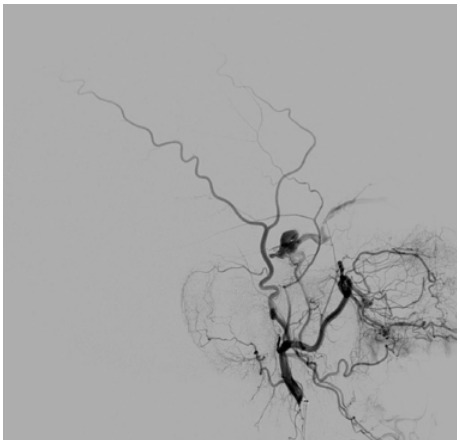

Figure 2: Location of the carotid cavernous fistula (arrow) Source of Photo: Courtesy of Radiology Department, Hospital of University Malaya).

procedure confirmed the material in the cavernous sinus. (Figure 5).

His condition improved later with

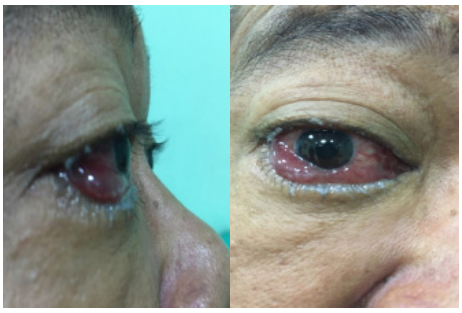

Figure 3: Lateral view and anterior view right eye

reduction of proptosis and chemosis 1-month post event (Figure 6). His vision however remained at hand movement in right eye. RAPD still present (Grade I) and IOP was 22mmHg on 3 types of antiglaucoma. Fundus showed cherry red spot with pale retina (Figure 7).

At 3 months post op, his condition was stable, and he was comfortable without any pain or redness to the eyes. His right eye visual acuity was 6/36, and the IOP was 18 mmHg, The Alphagan eye drop

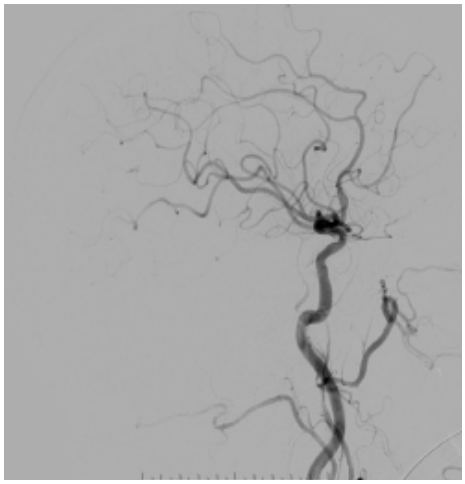

Figure 4: Obliteration fistula. Source of Photo: Courtesy of Radiology Department, Hospital of University Malaya.

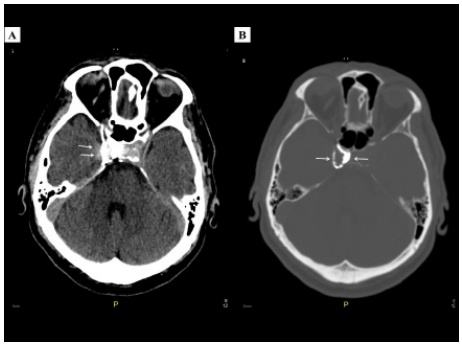

Figure 5: Non-contrast-enhanced computed tomography of the brain in axial images in (A) brain window showing artifact from the right cavernous sinus and in (B) bone window dense embolic material in the right cavernous sinus (Source of Photo: Courtesy of Radiology Department, Hospital of University Malaya).

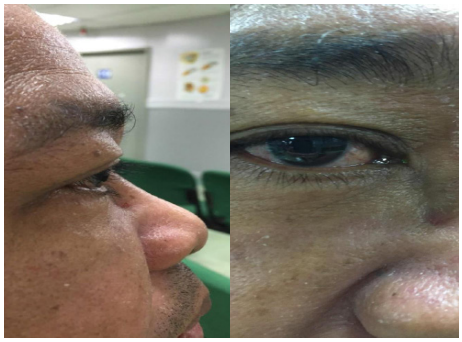

Figure 6: Lateral and anterior view of the right eye of the patient, 1 month after treatment, showing resolution of the chemosis and proptosis, but vision remains hand movement (HM)

was discontinued and he was seen again 4 months later (7 months post procedure). During this time, he denies any new complaints, the right eye visual acuity remained the same at 6/36 and his IOP came down to 14 and the timolol eye drop was discontinued. At 12 months follow up after the procedure, his best corrected visual acuity (BCVA) of the right eye improved to 6/24 and IOP is well controlled (15 mmHg) with single topical antiglaucoma

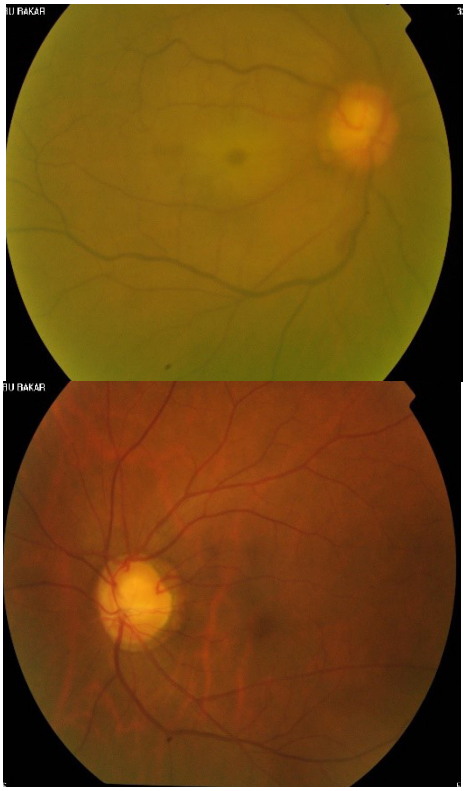

Figure 7: OCT macula of the right eye, showing cup disc ratio of 0.7, pale retina with cherry red spot as compared to the left eye.

Discussion

Carotid cavernous fistula (CCF) is an atypical communication between the carotid arterial system and the cavernous sinus. CCF can be classified on the basis of: (a) aetiology (spontaneous or traumatic), (b) hemodynamics (high and low flow) and (c) anatomy (direct and indirect). The most common classification is by Barrow et al,[4] who have divided CCF to 4 types according to its arterial supply:

Type A (direct): direct communication between the internal carotid artery (ICA) and the cavernous sinus.

Type B (indirect): supplied only by the dural branches of the ICA.

Type C (indirect): supplied only by dural branches of the external carotid artery (ECA).

Type D (indirect): supplied by dural branches of the ICA and ECA.

This classification is at present widely used and is of vital importance as the method of endovascular treatment may change. Angiography in this patient revealed that the fistula was supplied by dural branches of both ICA and ECA, therefore it was classified as Type D (indirect) CCF.

Unlike direct CCF, which mainly attributed by trauma, indirect CCF usually present with gradual onset of symptoms. Most of the symptoms are eye-related symptoms which include chemosis, exophthalmos, cranial nerve deficits, decrease in visual acuity, diplopia and ptosis.[2,3,5] This patient exhibited progressive sets of ocular of symptoms, which had threatened the vision of the right eye, and was complicated with secondary glaucoma.

In indirect CCFs, the goal of treatment is to reduce the pressure in the cavernous sinus by interrupting the fistulous communications. This can be achieved by obliterating the cavernous sinus that harbors the fistulous communication (transvenous embolization) which is more successful or obstructing the arterial branches that supplies the fistula (transarterial embolization).[1,6] Coils has been traditionally used in treatment of both direct and indirect CCFs. The benefits of coils are their radio-opacity and thrombogenicity which permits precise deposition and location into the cavernous sinus.[3] It is also easy to position and can be recovered if the initial location is not acceptable.[1] However, the coils need to be optimally packed to accomplish complete sealing which is difficult. Coils also tend to exert more mass effect, therefore dense packing of coils into the cavernous sinus may cause cranial nerve palsy. 'PHIL' (Precipitating Hydrophobic Injectable Liquid) (Microvention, Inc California, USA) is a recent advent of non-adhesive

liquid embolic agents. It has been recently used in treating indirect CCFs. Preliminary experience of its use in CCFs and spinal dural arterio-venous fistulas. appears to be an excellent embolic material with certain advantages compared with other available liquid embolic agents.[7]

In this patient, cerebral coiling was attempted but failed. Due to deterioration of the ocular signs (increasing proptosis, worsening vision, high IOP, presence of exudative retinal detachment and also CRAO), embolization using PHIL was then attempted to occlude the fistula, which was successful. However, the damage to the vision was severe and he had a vision of 3/60 in right eye 8 months' post event, which still need a single antiglaucoma eyedrop to maintain the IOP, although the proptosis and chemosis resolved.

Indirect CCF represent 10-30% of all CCFs, in which Type D is the commonest among the indirect CCF.[8] It is described as having a communication between one or more meningeal branches of external carotid, internal carotid artery or both and the cavernous sinus. In this form of fistula, the intra-cavernous portion of internal carotid artery remains intact. Arterial blood will flow via the meningeal branches of internal or external carotid arteries indirectly into cavernous sinus. Due to slow blood flow, the clinical features are subtler than in a direct fistula.[1]

The patients with CCF may present with chemosis, pulsatile exophthalmos and complaints of hearing a noise in the head. Clinically patients presented with corkscrew episcleral blood vessels in association with conjunctival chemosis, pulsating proptosis, thrill and bruit. These features should have a high index of suspicion of the diagnosis of arteriovenous fistula.[9] Resistance from the retrograde venous drainage into the ophthalmic vein may be causing proptosis, episcleral and conjunctival arterializations. Limited ocular movement and diplopia as a consequence of hypertrophied extraocular muscles; and exposure keratopathy as an effect of proptosis may present with a painful cranial nerve palsy with a white quiet eye in the absence of any proptosis.[10] The definite diagnosis can be confirmed by angiography, which may confirm a posterior draining CCF. Elevated episcleral pressure and vortex venous pressure may result in elevated intraocular pressure (IOP) and secondary glaucoma.[11] One of the often-observed ocular manifestation of CCF is secondary glaucoma, and closing the fistula is the crucial for satisfactory IOP control. There may be decreased ocular and retinal perfusion resulted by venous and arterial stasis. Retinal and choroidal changes may include, retinal hemorrhage, venous dilatation, CRAO, CRVO, cotton wool patches and serous retinal detachment. In addition, decreased perfusion to intra-cavernous sinus cranial nerves may cause anterior segment ischemia, causing ophthalmoplegia and diplopia mimicking Graves' ophthalmopathy. The visual loss may be secondary to corneal, retinal or optic nerve changes or may result from the accompanying glaucoma.[12] Rarely, a case of CCF after a cataract surgery has been reported.[13]

Embolization of CCF may carry a risk of inherent complication either from the procedure or due to reopening of the fistula. Complete ophthalmoplegia and visual acuity loss due to a central retinal vein obstruction (CRVO) after an attempt to close a CCF has been reported.[14] Ophthalmic artery occlusion and cerebral infarction post embolization are rare, which is one study reported 3 in 80 treated patients suffered such complications.[8] Other complications include increased proptosis, elevation of IOP, choroidal detachment, venous stasis retinopathy, ophthalmic vein thrombosis resulting in CRVO and neovascular glaucoma after embolization attempt.

Most CCFs are vision threatening, although they are usually not life threatening. Main indications for treatment include diplopia, glaucoma, intolerable headache or bruit, and severe proptosis producing exposure keratopathy. Spontaneous closure from thrombosis of cavernous sinus is unlikely. Non-surgical approach includes carotid compression therapy while surgical management includes ligation of the external and internal carotid arteries; and fistula embolization with particles, glue, detachable balloons and thrombogenic microcoils. Treatment of cavernous dural arteriovenous fistulas is usually done using a trans-arterial approach, in which in this patient done via the femoral artery and the external carotid artery, was successful and showed complete obliteration of the fistula.

The role of ophthalmogist is very important in this type of cases, as many patients with CCF may initially present to an ophthalmologist. High index of suspicion, appropriate diagnostic investigation is important to make a correct diagnosis. Proper follow up and care must be delivered to the patient as these patients might develop complications such as CRAO and secondary glaucoma.

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Case series: the rise of fungal endophthalmitis from suspected environmental contamination

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Background: A spike of 5 cases of positive culture fungal endophthalmitis occurred within a period of 30 days in patients with different working diagnosis. Investigations were initiated to look for possible causes/explanation.

Results: Five cases with different working diagnosis had positive fungal culture within a period of thirty days. Investigations showed that four out of five sampling were done in the same procedure room, and that all culture plates used were from the same refrigerator in the same procedure room. The procedure room environment was sub-optimal for procedures. A non-functioning air-conditioner created a hot and humid environment. A blowing stand-fan was used to provide air circulation during procedures. Multiple green-black-brownish spots of fungi growth were noticed on the cellulose ceiling board. The infection control team were informed and involved in investigation and rectification process, which include but not restricted to thorough disinfection procedures and air-conditioner repair. There were no longer any clinically inappropriate positive cultures reported following rectification. As patients responded well without/before starting anti-fungal therapy, we strongly believe that the clinically inappropriate positive cultures were due to environmental contamination.

Conclusion: Contamination/infection can occur via airborne pathogen transmission especially fungi, thus WHO recommended a level of <50 CFU/m^3 of air in hospital settings. A high level of suspicion should be maintained. Lab results are not absolute and clinical co-relation is of utmost importance in patient's management.

Conflicts of interest: The authors report no conflicts of interest.

Keywords: Endophthalmitis, fungi, air contamination, false positive culture.

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Introduction

Fungal endophthalmitis is an uncommon but severe sight-threatening ocular emergency that requires immediate treatment. Post-operative fungal endophthalmitis has a low rate of less than 1%.[1] Post intravitreal

injection fungal endophthalmitis ranges from 0% to 4%.[2,3] Endogenous fungal endophthalmitis from fungaemia has a rate of only 1.6%.[4] It is thus rare to see a sudden spike of five cases of culture-positive fungal endophthalmitis within a 30 days period, especially when these cases already had a more clinically relevant working diagnosis. Investigations were then carried out together with the hospital infection control team to identify the possible explanation or causes.

Materials and methods

This is a case series made up of five cases. We proceeded with retrospective analysis of the five cases. We investigated the first contact with the patient, history, clinical course, procedures, treatment and treatment outcome. The infection control team was also involved in our investigation, where they were involved in assessing the room with suspected contamination, which include environmental sampling for cultures and the subsequent rectification procedures. There is no conflict of interest involved in any way in the preparation of this case series.

Results

Five cases are summarised individually and listed in a chronological order. Investigation findings will also be listed, followed by solution and outcome. All positive cultures in the lab were immediately sent to Institute of Medical Research, Malaysia for continuation of culture and species identification.

First case

A 50-year-old lady with underlying bronchial asthma complained of blurring of vision in the left eye for 2 months duration associated with red eye. There was no pain, entrance of foreign body, discharge or history of trauma prior to the symptoms. She had no recent contact with any patients with red eye, but she did have TB contact history with both her parents who were previously treated as pulmonary tuberculosis 2 years ago. Her father defaulted treatment due to compliance issue, and the mother died of complication from tuberculosis infection. Visual acuity of the left eye at presentation was CF (counting finger) at 1-foot. Examination showed injected left eye, anterior chamber cells of 4+ with mutton fat keratoprecipitates and posterior synechiae. Fundus examination was hazy due to vitritis and poor pupil dilatation, with B-scan showing posterior vitreous detachment, vitritis and flat retina but no loculation. Investigations showed a raised ESR at 39mm/hr, as well as a significant Mantoux test induration of 28mm. Other infective screenings were negative. She was then treated as presumed ocular TB and was started on anti-TB treatment, planned for a total duration of at least 9 months. Following anti-tuberculosis treatment, together with topical steroid and homatropine, vision improved to CF 2-feet, but only mild improvement in anterior chamber activity, with cells 3+ and no hypopyon. She then underwent an anterior chamber tap in procedure room 6B under aseptic technique, followed by intracameral recombinant tissue plasminogen activator and moxifloxacin injection. The anterior chamber tap was sent for culture, gram staining and KOH staining, but insufficient to be processed for TB PCR. Topical moxifloxacin was added on top of the steroid following the procedure. Inflammation continued to improve, and topical steroid was reduced. However, subsequent review in clinic noted positive fungal culture (later identified as non-sporulating hyaline mold) from the anterior chamber tap. A vitreous tap and intravitreal injection of ceftazidime 2mg/0.1ml, vancomycin 1mg/0.1ml and amphotericin B 0.005mg/0.1ml was given in procedure room E16. She was also started on oral fluconazole 200mg BD, topical fluconazole 0.2% and topical amphotericin

B 0.15%. Anti-TB, topical steroids and topical moxifloxacin were continued, and she was also planned for diagnostic and therapeutic vitrectomy. Patient however was lost for follow-up since then, and defaulted admission for the surgery.

Second case

An 18-year-old girl was admitted to the medical ward and was being treated for multi-drug resistant organism Acinetobacter baumannii sepsis (blood). She was referred to the ophthalmology team for complaint of blurring of vision in her right eye. Visual acuity of the right eye was CF at 1-foot, left eye was 6/6. Right eye showed a white conjunctiva and anterior chamber has cell count of 2+ with no hypopyon. Fundus examination showed a localised and well-defined yellowish abscess measuring about 1/3 optic disc diameter covering the fovea. Vitreous showed minimal localised vitritis overlying the abscess. B-scan done showed vitreous loculation. She was treated as endogenous endophthalmitis. Vitreous tap was taken prior to the first intravitreal antibiotic injection of (ceftazidime 2 mg/0.1ml and vancomycin 1mg/0.1ml). The tap and injection were performed in procedure room 6B under aseptic technique. Following the procedure, she was started on oral ciprofloxacin 750mg BD and topical G. Moxifloxacin 0.5% and G. Dexamethasone 0.1% hourly round the clock. She was given again on day 3 of treatment, while awaiting vitrectomy. Day 6 into treatment, the vitreous tap culture came back as positive for fungi (later identified as non-sporulating hyaline mold). Patient showed clinical improvement on antibiotics alone, with less vitritis, even though the abscess size remained similar and well defined. A repeated B-scan on day 7 no longer showing any loculation. In view of the positive fungal culture, intravitreal Amphotericin B was given on top of intravitreal ceftazidime and vancomycin at day 7. Systemic anti-fungal with oral voriconazole 200mg BD was then initiated as suggested by the infectious disease team. Topical G. Amphotericin B 0.15% and G. Fluconazole 0.2% was started 2 hourly. Patient no longer receive any intravitreal injection until she undergone vitrectomy on day 13 in order to remove the sub-inner limiting membrane abscess. Repeat vitreous biopsy was taken intra-op and sent for culture. Intravitreal antibiotic and anti-fungal was given at the end of the surgery. She was kept on topical steroid, topical antibiotic, topical antifungal and systemic fungal post-vitrectomy. The repeated vitreous sampling taken intra-op in the operating theatre came back negative for any culture. Her vision recovered well since surgery with a final vision of 6/9.

Third case

A 61-year-old Chinese lady with underlying hypertension, diabetes and dyslipidemia referred from private clinic with right eye vitreous haemorrhage of unknown cause for 2 months duration. The blurring of vision was painless and of sudden onset. On examination, the vision was hand movement. The anterior segment was unremarkable. There was no fundus view with B-scan showed a flat retina with vitreous haemorrhage. The examination of the other eye was otherwise normal. She underwent right eye vitrectomy for prolonged vitreous haemorrhage. Intra-operatively, the retina and macula were flat. Inferior retinitis, temporal necrotic retinitis, vasculitis and multiple yellow-white retinal deposits resembling the clinical picture of acute retinal necrosis was observed. Vitreous sample was then taken intra-op (half-way into vitrectomy) and sent for culture, cytology, viral PCR (polymerase chain reaction) and tuberculosis PCR. Her vision immediately improved to 6/18 following the surgery, before the recurrence of vitritis on day 3 post op with viral PCR result positive for VZV

(varicella zoster virus). She was treated as acute retinal necrosis and was started on intravenous acyclovir 750mg TDS therapy day 3 post vitrectomy. Her vision improved from hand movement only to 6/9 with improving inflammation within 3 days of starting intravenous acyclovir. Her antiviral therapy was forced to stop 3 days after due to deteriorating renal function. Day 7 post vitrectomy, the same vitreous sample (positive of VZV PCR) from the operating theatre was reported to have a positive fungal culture growth, which later was identified as non-sporulating dematiaceous mold species. It is worth mentioning that even though sampling were done under aseptic technique in operating theatre, culture plates used were kept and sent to operating theatre from procedure room 6B. With the positive fungi culture, she was added on with topical anti-fungal, G. Amphotericin B 0.15% 2 hourly and G. Fluconazole 0.2% 2 hourly, despite the improvement seen on antiviral treatment. Patient continued to improve clinically with topical treatments only and steroids were gradually tapered. Unfortunately, patient developed retinal detachment 3 weeks post vitrectomy, a classical common complication of ARN, before systemic acyclovir could be restarted. She had then undergone repeated VR surgery with endolaser and silicon oil tamponade. Following the removal of silicon oil after 5 months, her right eye vision remained stable at counting finger 2-feet.

Forth case

A 59-year-old lady with underlying diabetes, hypertension and dyslipidemia, complained of progressive eye pain and redness 2 days after her right eye intravitreal ranibizumab for central-involving diabetic macula edema. She presented 15 days after the injection with a visual acuity of hand movement on the right eye. Examination showed an injected right eye. The cornea was hazy with thick hypopyon covering lower half of the anterior chamber. Fundus view was poor with B-scan showed loculations in the vitreous. A diagnosis of exogenous endophthalmitis was made and a vitreous tap was performed immediately in procedure room 6B under aseptic technique, together with intravitreal ceftazidime 2mg/0.1ml and vancomycin 1mg/0.1ml injection. Straw colored vitreous tap was obtained and was sent for culture and staining. She was then started on topical moxifloxacin 0.5% and topical dexamethasone 0.1% every hourly round the clock. Oral ciprofloxacin 750mg BD was also started. Patient underwent right eye cataract removal, vitrectomy, silicon oil tamponade and intravitreal antibiotic injection 3 days later (before culture result). Intra-operatively, extensive vitreous and pre-retinal abscess were seen and removed, with sample taken intra-op for repeat culture. Retina and macula were flat. Her topical antibiotic and steroid were continued hourly round the clock after the surgery. 2 days after surgery, initial culture result (taken in room 6B) came back with positive mold (unable to specify species) culture. Two hourly topical fluconazole 0.2% and amphotericin B 0.15% were added. 6 weeks of oral fluconazole 200mg BD was also started. Vitreous culture sent from operating theatre did not grow any organism. Patient's vision improved to 6/60 before patient subsequently developed retinal detachment with silicone oil in situ 3 months after surgery, with vision drop to hand movement only.

Fifth case

A 62-year-old gentleman with underlying diabetes, hypertension and bronchial asthma was referred from private center for continuation of care for acute post-operative methicillin- resistant staphylococcus aureus endophthalmitis. Patient underwent uncomplicated left eye phacoemulsification.

His surgery was complicated with acute post-operative MRSA endophthalmitis (vitreous culture). He was given total 3 intravitreal vancomycin injections and loaded with intravenous vancomycin in the private center, and he responded well with resolution of hypopyon. Upon admission, he presented with a left eye vision of counting finger at 1-foot. The left eye had injected conjunctiva and the cornea was edematous. Anterior chamber showed cells 2+, keratoprecipitates on endothelium without hypopyon. PCIOL was stable. There was no fundus view with B-scan showed a dense loculation near the posterior pole. A vitreous sampling for culture was performed prior to our intravitreal vancomycin. The sampling was done in procedure room 6B under aseptic technique. He was started on topical vancomycin and topical prednisolone 1% every 2 hourly on the left eye. Intravenous vancomycin 15mg/kg BD was started and planned for a total of 6 weeks as advised by the infectious disease team. 3 days after admission, vitreous culture taken on admission showed positive fungal growth identified as Geotrichum species later. Patient was then added on topical fluconazole 0.2% and topical amphotericin B 0.15% every 2 hourly in addition to the topical vancomycin and steroid. One dose of intravitreal amphotericin B 0.005mg/0.1ml was given before his vitrectomy 2 weeks later. Oral voriconazole 200mg BD was also started by the infectious disease team and was planned for a total treatment of 6 weeks but it was discontinued by our treating consultant after 12 days of treatment. Intra-operative finding during vitrectomy showed vitritis, with retina and macula flat. Vitreous sampling was done and sent for culture and staining. Intravitreal vancomycin 1mg/0.1ml and amphotericin B 0.005mg/0.1ml was given at the end of surgery. At this point of time, patient received 7 doses of intravitreal vancomycin and 2 doses of intravitreal amphotericin B. Patient was kept on topical vancomycin, anti-fungal, steroid and chloramphenicol after the surgery. Vitreous sample taken intra-operatively showed no pus cells, and no culture was isolated. Topical anti-fungal was stopped 2 weeks after vitrectomy. Patient was only on topical steroid and topical vancomycin, tapered over time. Patient's vision improved to 6/24 two weeks after the vitrectomy. Upon completion of 6 weeks of intravenous vancomycin, patient's vision further improved to 6/18. He was discharged with topical prednisolone 1% and vancomycin 6 hourly. His vision further improved to 6/6 1 month after discharge. All medications were stopped since then and he then defaulted subsequent follow ups.

From the cases above, it was clear that most of the cases above do have their own working diagnosis with strong clinical and laboratory evidence. However, the positive fungal culture had caused some distraction and minor deviation on the initial treatments which were effective, proven by clinical improvement on these patients. Though anti-fungal therapy was initiated, and mostly are incomplete therapy, the clinical course of these patients subsequently developed towards the direction of its own initial diagnosis, rather than a fungal endophthalmitis. This strongly suggests that the positive cultures were contaminations.

Discussion

Fungal endophthalmitis is uncommon compared to bacterial endophthalmitis.[1-4] The presence of five cases within a period of 30 days is extremely rare.

Four out of five cases mentioned had the positive sampling done in procedure room 6B, under aseptic technique and by different operators (ophthalmology trainees and specialist), with all five cases had the culture plates originated from procedure room 6B. While each cases above already had a working diagnosis with positive

evidence (ocular tuberculosis, endogenous bacterial endophthalmitis, acute VZV retinal necrosis, post intravitreal injection bacterial endophthalmitis and MRSA endophthalmitis), and they were responding to treatment, culture results were still pointing towards fungal endophthalmitis with the positive culture. It was already mentioned that fungal endophthalmitis is uncommon itself, it is even more rare to have a sudden surge of five cases within a range of 30 days. This led to the suspicion of contamination and thus investigations were commenced.

When contamination was suspect, it was almost always first linked with the procedure and operator. Contact contamination are usually the commonest during procedure. However, in our series, the procedure was done properly by ophthalmology trainees/ specialist and were all performed by different operators and thus the chance of improper procedure handling in each and all cases was small.

Environmental contamination was then suspected in our series, given the fact that four out of five cases had the sampling done in the same procedure room, with all the culture plates used in all five cases were kept in the refrigerator within the same room. A joint investigation was then conducted on the procedure room together with the hospital infection control team.

Following the investigation, it was noticed that the procedure is of hot and humid environment with non-functioning air-conditioner. A stand-fan was present to provide air circulation during procedure and there were no windows available. The procedure room was not reserved for ophthalmic procedures and sterile sampling, but also for ECGs, blood taking and vision taking (high volume of personnel entering the room). There was prominent fungal growth on the cellulose ceiling tiles in the room.

Figure 1: This picture shows the cellulose ceiling board in procedure room 6B. It was stained brownish by watermark, and the black-green patches were foci of fungal growth. The ceiling board was eventually replaced during rectification process.

The culture plates used in all cases were kept in the refrigerator inside the procedure room. There were also pooling of water noted around the air-conditioner vent on the ceiling and the water was taken for culture. Unfortunately, there were no direct sample taken from the fungal infested ceiling tiles for culture. Air culture was also not obtained due to the lack of appropriate equipment.

It is important to remember that fungi can survive in almost any environmental conditions, given their high adaptation ability to the environment.[5] They have multiple modes of reproduction and via multiple routes, which include air transmission via spores. Though the cultures obtained in our lab culture were mostly identified as non-sporulating species, but we must remember the basic of mycology, that certain dimorphic fungi like dematiaceous species are able to switch between sporulating and non-sporulating mode depending on the surrounding conditions like circulation, type of nutrients and temperature etc.[5] Fungi spores are almost always available in the air, both outdoor and indoor, even in conditions where no obvious sources are seen, not to mention when there

is a visible source available.[6,7]

In fact, the health threat posed by indoor fungi spores is real.[7] This has led to the development of multiple recommendations by different organizations for a safe level of indoor air fungi concentration. Due to the presence of multiple guidelines and no general consensus on which shall be the standard reference, we are referring to WHO guideline of recommendation for the acceptable level of air-borne fungi in the building published in the year 1988, where it recommends an air-borne fungi level of not more than 50CFU/m3 of air in hospital settings.[8] However, many people including healthcare personnel are not aware of its presence and importance. Air sampling was also rarely performed in our settings for it requires sophisticated air impactor for sample collection.

Studies have been conducted overseas to determine the indoor air quality of various buildings and hospitals, looking at the amount of fungi in the air. Often the fungi spore density in the air is way above the recommended level, including clean rooms in hospital.[9-12] In places with different seasons, it is during summer and autumn, where temperature is higher and more humid, had a higher concentration of air-borne fungi.[13] In tropical country like Malaysia, where the weather is persistently warm and humid all year long, air-conditioner helps reduces the indoor air fungi load.[11] Under the proper environment, fungi can easily grow on any surface. The exposure of the culture plates by just few seconds is enough for air contaminants to land, especially when the load is high in the air with turbulent air flow (which in our series, a stand-fan aiming at the procedure was present).[14]

Though unfortunately the culture came back negative of growth for samples taken from the air-conditioner vent swab and the pool of water near the air-conditioner vent (the only 2 samples taken, ceiling tiles were omitted), thorough terminal cleaning of the room was ordered by the infection control team and were done twice.

Surface cleaning (including table surface, bed, trolleys, refrigerator, floor, walls, cabinets, etc.) of the room were done twice, with each session involved the usage of Savona D2 (alcohol-based disinfectant) and Germicep (chlorine-based disinfectant). Air-conditioner were repaired promptly, and strict room temperature monitoring was initiated. The ceiling tiles infested with fungi were replaced. Curtains were also changed as part of the terminal cleaning procedure. Limitation of personnel entering the room was enforced, where the room is strictly reserved for clean and sterile clinical procedures. Thermometer was also installed in the room for continuous temperature monitoring.

Following the rectification processes, there was no longer any clinically inappropriate culture growth results obtained. This strongly suggests that the previous surge of positive cultures were contamination from the environment, supported by the fact that patients responded well before and/or without proper anti-fungal therapy.

From the experience gained through our case series, it is imperative for all clinicians to be more conscious of their clinical environment prior to any procedures, especially invasive procedures and surgeries. Environment cleanliness should be maintained by regular and thorough cleaning with the appropriate disinfectants. Disinfection should not be confined to the working area and surfaces but also electrical appliances and storages. Surrounding temperature and circulation problems should not be neglected as it contributes to transmission of airborne pathogens and may cause contamination. Most importantly, maintain high sterility during procedures to protect patients and avoid contamination. Most importantly, always remain suspicious when there is a sudden spike of inappropriate positive

cultures, as contamination can happen not only during procedure, but it also occur in, or brought into the laboratory itself.[15]

Conclusion

In conclusion, contamination of lab cultures are most commonly assumed to be contact contamination during procedures. Environmental contamination was often overlooked but it should always be suspected when a clinically inappropriate positive culture is obtained. It was always a spinal reflex to attribute any suspected contamination to improper technique during procedure. By maintaining a high level of suspicious and carrying out prompt investigations such as those demonstrated in this case series, the real cause of contamination could be identified early with proper management could be arranged. This would prevent patient mismanagement, and avoid more cases of contaminations. More importantly, management of patients should always co-relate clinical findings with history, and never solely based on lab investigations. Treatment based on lab results alone could bring more harm than benefits to patients. Strict adherence to sterile technique during sampling and procedures are no longer the only precautions which requires attention. Environmental factors like Indoor air quality and cleanliness are equally important and should never be overlooked. Transportation and storage of culture medias should be given equal emphasis. When multiple contamination is suspected, thorough investigations should be conducted and environmental factors such as humidity, air-circulation, temperature etc. should never be neglected.

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Epithelial inclusion conjunctival cyst after strabismus surgery - a rare occurrence

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Background: Epithelial inclusion conjunctival cysts are a rare occurrence post strabismus surgery. These cysts if left untreated can enlarge and cause complications such as limitation of eye movements, strabismus, proptosis and compression of ocular structures. Here we present a case of epithelial inclusion cyst post routine medial rectus recession, which was successfully treated with surgical excision.
Methods: Case Report
Results: A 4-year old Malay girl with partially accommodative esotropia underwent uneventful bilateral medial rectus recession. Post-operatively 4 months later, she developed nasal conjunctival mass of her right eye. The conjunctival mass was unresponsive to topical steroids and surgical excision was performed. Histopathological examination confirmed the mass as epithelial inclusion cyst.
Conclusion: Prompt diagnosis and management of epithelial inclusion cyst is crucial to prevent subsequent ocular complications.
Conflicts of interest: The authors report no conflict of interest.
Keywords: Conjunctival cyst, epithelial inclusion cyst, strabismus surgery
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Background

Epithelial inclusion cysts are membranous structures lined with epithelium. These cysts typically contain fluid, which may be serous, necrotic or haemorrhagic in nature. The development of epithelial inclusion cysts following ocular surgery is rare. Various factors contributing to cyst development include implantation of conjunctival epithelium in the surgical wound, infection or chronic immune reaction to sutures.[1] Ocular surgery where there is breech to the conjunctiva and sclera increase the risk of development epithelial inclusion cysts. These surgeries include strabismus surgery, retinal detachment surgery, orbital surgery and ptosis repair.[2-4] Epithelial inclusion cysts can range from small conjunctival cysts to large orbital masses. Aside from cosmetic appearance, these cysts may infiltrate the layers of the conjunctiva,

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muscle and sclera to cause limitation of eye movements, strabismus, astigmatism, amblyopia, proptosis or compression of ocular structures from mass effect.[5,6] In view optimal treatment is necessary to prevent cyst progression and recurrence, we aim to present a case of epithelial inclusion cyst post strabismus surgery, which was successfully treated with surgical excision.

Case history

A 4-year old Malay female with partially accomodative alternating esotropia of 30 prism diopters underwent uneventful bilateral medial rectus recession of 4.5mm through limbal conjunctival incision. Vicryl 6/0 was used to secure the medial rectus and the conjunctiva. Post-operatively patient was doing well. Four months later, the patient's parents noticed a lump in patient's right eye, which progressively increased in size.

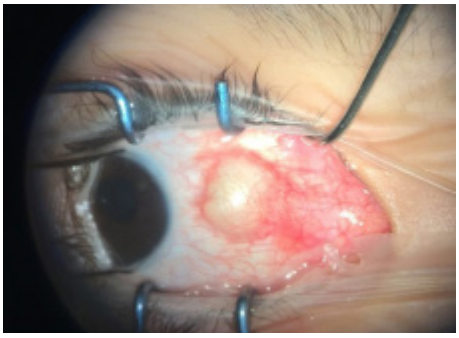

Figure 1: Pre-excision of cyst (Right eye)

On examination, best-corrected visual acuity was 6/6 in both eyes and patient was orthophoric. Ocular motility was normal and no proptosis was noted. Inspection of the right eye revealed a nasal conjunctival mass measuring 3 mm in diameter, which did not transilluminate. No inflammation of the conjunctiva was noted and examination of other areas of the eye was normal. Examination of the left eye was unremarkable. The patient was started on topical Maxitrol (Neomycin, polymycin B sulphate, dexamethasone 0.1%) eyedrops four times a day for one month.

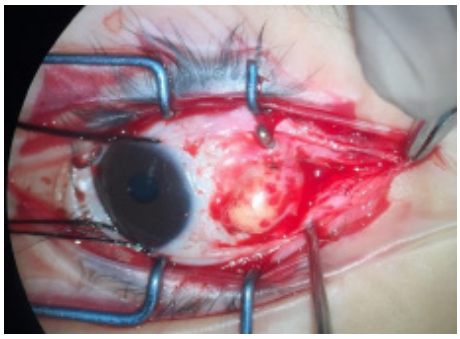

Figure 2: Excision of conjunctiva revealing the cyst intraoperatively

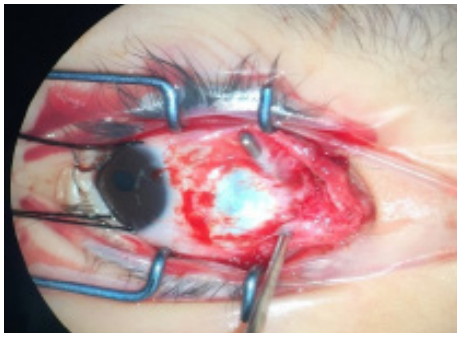

Figure 3: Post cyst excision, removed in-toto

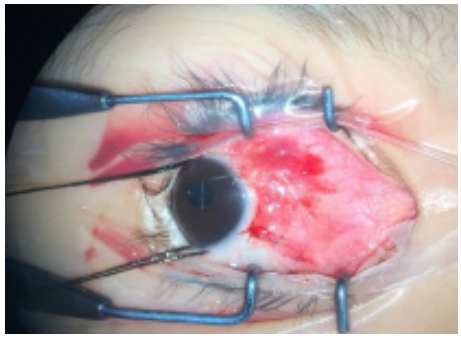

Figure 4: Wound closed completely the cyst intraoperatively

The conjunctival mass however did not resolve and surgical excision was carried out. Intra-operatively, the mass was densely adherent to surrounding conjunctiva and sclera and located at the insertion of the medial rectus. The mass was excised in toto and measured 5.0mm x 5.0mm x 3.0mm. Post-operative review showed complete resolution of the lesion with no complications. Patient remained orthophoric and has been well at 6-months post cyst excision.

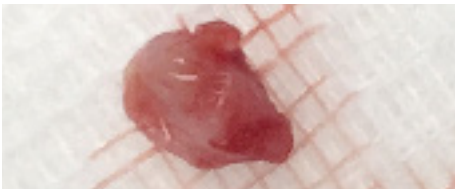

Figure 5: Macroscopic appearance of excised cyst with cyst wall intact the cyst intraoperatively

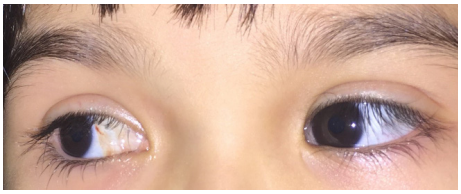

Figure 6: Right eye appearance post operatively 1 month

Histopathological Analysis

Histopathological examination reported dense fibrotic tissue surrounding a cystic structure which was lined by conjunctival epithelium. Findings were consistent with conjunctival epithelial inclusion cyst.

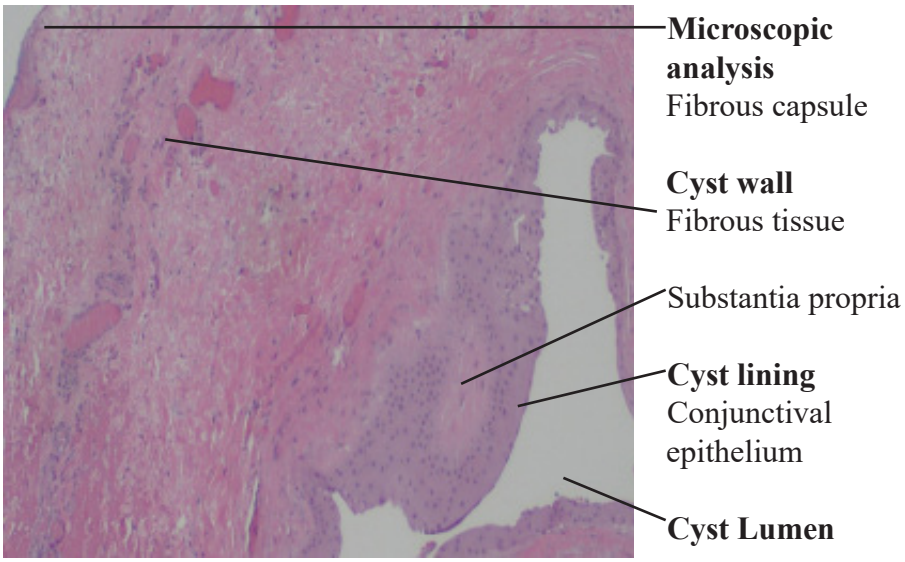

Image Details

Stain: Hematoxylin & Eosin (H&E), Magnification: X 40, Microscope: Olympus CX33

Discussion

The incidence of epithelial inclusion cysts is reported to range from 0.25% to 0.4% of strabismus surgery.[1,7] The duration to development of the cysts can range from a few days to 70 years post-operatively.[8,9] Our patient shared a similar time-frame with a previous case report series of three patients by Anjali et al who reported the appearance of cyst at 2 - 4 months.[10] Our case corresponded to reported literature where it was reported rectus recessions were associated with an increased incidence of cyst formation.[7] Treatment of

conjunctival epithelial inclusion cysts can be divided into non-surgical and surgical options. A trial of steroids is the first-line treatment as some cysts may resolve spontaneously.[8,11] Persistent large cysts however would require surgical intervention.

Surgery for epithelial inclusion cysts include injection of isopropyl alcohol, thermal cautery, marsupilization and excision in toto.[8,12,13] Though complete excision is preferred, surgery for epithelial inclusion cysts can range from straight-forward surgical excision to partial cyst excision with possible spillage of cyst contents into neighboring structures. In addition, extraocular muscles may inadvertently be cut and globe perforation may occur during cyst excision as the cyst may be deeply embedded in the muscle or sclera. This is due to the aggressive invasion of nearby ocular structures such as extraocular muscles and sclera by the cysts, which makes it difficult to visualize and define the cyst borders. In this case, we took precautions to isolate the medial rectus before cyst excision and the cyst could be excised in toto as it had not invaded the medial rectus. No data exists regarding the recurrence rate post cyst excision however it is recommended that these patients be followed up yearly.[6]

Conclusion

Epithelial inclusion cysts can occur due to various causes and the duration of development varies between cases. Successful diagnosis and treatment is crucial to prevent subsequent ocular complications. To our knowledge, this is the first case report of its nature from Malaysia and we hope that the findings of this case will contribute to better understanding of this condition.

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Ocular infection with cytomegalovirus in Thailand: the clinical features, treatments and outcomes

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Purpose: To study the clinical features, treatments and outcomes of ocular cytomegalovirus (CMV) infection.
Methods: Retrospective case series. Medical records of patients who had ocular CMV infection treated at Thammasat university hospital, Thailand from January 2015 to May 2017 were included. Clinical features, treatments and outcomes were analyzed.
Results: Forty-one patients were diagnosed with ocular CMV diseases including infection in immunocompetent patients (n=25, 61%) and infection in immunocompromised cases (n=16, 39%). Among the immunocompetent group, anterior uveitis was the most common manifestation (n=22, 88%). Posner Schlossman syndrome (n=14, 56%) was the majority of CMV anterior uveitis cases. Patients with CMV anterior uveitis had iris atrophy in 90.5% of cases, increased intraocular pressure in 88% of cases, decreased endothelial cell count in 38.1% of cases and coin-shaped lesions in 27.3% of cases. Anti-viral therapy was administered in 88% of cases and 64% of cases needed long-term topical corticosteroids. Most immunocompromised patients were diagnosed with CMV retinitis (93.8%). Almost all patients (n=14, 87.5%) had HIV infection. Immune recovery uveitis developed in 20%. Five cases (31.3%) of CMV retinitis received intravenous ganciclovir with adjunctive intravitreal injections of ganciclovir while 68.8% of cases were treated with only intravitreal injections of ganciclovir. Most patients well responded to treatment with the mortality rate of 6.3%.
Conclusions: Cytomegalovirus can infect both immunocompetent and immunocompromised host with variety of clinical features. Anterior uveitis was common in immunocompetent cases while retinitis was common in immunocompromised patients.
Conflicts of interest: The authors declare no conflict of interests.
Keywords: Cytomegalovirus, anterior uveitis, retinitis, endotheliitis
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Introduction

Cytomegalovirus (CMV) is a large-enveloped double-stranded DNA virus in Herpesviridae family, which can be transmitted by saliva, breast milk, sexual contact and organ transplantation.

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Both immunocompetent and immunocompromised host can be infected by CMV in any age group.[1-4]

There are many clinical features caused by this virus which may affect anterior segment, posterior segment or both.[5-7] These diseases vary in severity, from spontaneously resolved to severe visual impairment if the patients were not treated promptly and properly.[8-15]

Our interest was in the variation of clinical features of ocular CMV infection,

therefore the main objective of our study was to report the characteristics of the patients, symptoms, clinical manifestations, treatments and outcomes of this viral infection. From the best of our knowledge, there was no article studying various ocular CMV diseases in both immunocompromised and immunocompetent patients. In this case series, we described these aspects of CMV infected patients treated in Thammasat University Hospital, Thailand.

Methods

We performed a retrospective case review from documented medical records of patients who had ocular CMV infection treated at Thammasat University Hospital from January 2015 to May 2017. Our study was approved by the Human Research Ethics Committee of the Faculty of Medicine, Thammasat University, Pathum Thani, Thailand. Forty-one patients diagnosed with CMV-related diseases were enrolled in this study. Intraocular fluid qualitative polymerase chain reaction (PCR) was performed in all cases of anterior uveitis, intermediate uveitis and acute retinal necrosis and the results yielded CMV. However, CMV retinitis was clinically diagnosed without PCR technique. We excluded the patients who were misdiagnosed with CMV infection but subsequently found to have other specific diseases.

After enrollment, the characteristics of the patients; age, gender, medical illness, immune status, laterality, signs and symptoms, investigations, treatments and outcomes including complications were documented. All data were analyzed using an excel spreadsheet (Excel 2010; Microsoft Corp., Redmond, WA) and reported in term of means, standard deviations and percentages.

Results

Patient characteristics

Forty-one patients diagnosed with ocular CMV diseases were enrolled in this study. We excluded a patient who was initially misdiagnosed with CMV retinitis but subsequently found to have Behcet's disease. There were 25 immunocompetent patients (61%) and 16 immunocompromised patients (39%). The mean age of the patients was 44.9 years (24-67 years in range) and most of them were male (n=32, 78%). In the immunocompromised group, there were 14 human Immunodeficiency virus (HIV)-infected patients (87.5%), 1 systemic lupus erythematosus (SLE) patient (6.3%) and 1 diffuse large B-cell lymphoma patient (6.3%).

Clinical manifestations

The most common presentation was blurred vision (n=24, 58.5%) with various visual acuity. The majority of the patients had best-corrected visual acuity at baseline better than 20/40 (n=29, 70.7%). Other presenting symptoms included eye pain (n=6, 14.6%), red eye (n=1, 2.4%) and floaters (n=1, 2.4%). There were 2 asymptomatic patients (4.9%) and 7 patients (17%) that we could not find records about their presenting symptoms. CMV-related diseases reviewed in our study were unilateral (n=27, 65.9%) rather than bilateral (n=14, 34.1%).

Among the immunocompetent group (n=25), anterior uveitis was the most common manifestation (n=22, 88%), followed by posterior uveitis in 8% (n=2: 1 CMVR, 1 ARN) and intermediate uveitis in 4% (n=1). Posner Schlossman syndrome (PSS, n=14, 56%) made up the majority of CMV anterior uveitis (Table 1). Other clinical manifestations of CMV anterior uveitis included Fuchs heterochromic iridocyclitis (FHI), endotheliitis and combined PSS and endotheliitis. Patients presented with diffused iris atrophy in 90.5%, increased intraocular pressure in 88%, decreased endothelial cell count in 38.1% and coin-shaped lesions in 27.3% of cases.

In this study, almost all CMV retinitis was found in immunocompromised patients (n=15, 93.8%) which all cases were presented with fulminant (classic) form. Almost all immunocompromised patients (n=14, 87.5%) were HIV infection with the mean CD4+ T cell count of 62.7 cells/μL (range 1-163 cells/μL). Nine (64.3%) of

14 HIV-infected patients already received highly active antiretroviral therapy before presentations of ocular diseases. There were 2 patients (14.3%) whom first diagnosed HIV infection from ocular symptoms. Three patients with HIV infection came to eye clinic for screening CMV retinitis prior HAART initiation and they were found to have CMV retinitis. Immune recovery uveitis (IRU) was developed in 3 HIV-infected CMV retinitis patients (20%) which 2 cases presented with unmasking CMV retinitis and 1 case presented with paradoxical worsening of known CMV retinitis.

Treatments and outcomes

In the CMV-related anterior uveitis group, anti-viral therapy was administered in 86.4% of cases (n=19). Three cases were controlled by topical corticosteroids without antiviral therapy (2 PSS, 1 FHI). Antiviral therapy included topical ganciclovir (0.15% ganciclovir gel or 2% ganciclovir solution), valganciclovir, intravenous ganciclovir and intravitreal ganciclovir. All cases used topical corticosteroids for controlling inflammation. The diseases can be controlled by topical corticosterioids without anti-viral therapy in 3 patients (13.6%). Among the patients who received anti-viral therapy in anterior uveitis group (n=19), only 2 patients (10.5%) were able to stop using anti-viral agents and topical cortocosteroids (quiescence period: 2 years and 5.5 years). Five patients (26.3%) had recurrences after cessation of anti-viral agents. Twelve patients (63.2%) never discontinued anti-viral therapy because inflammation occurred after reducing the dose of topical corticosteroids or antiviral therapy. A patient with CMV anterior uveitis received an intravitreal injection of ganciclovir (4 mg/0.04 cc) due to unavailability of topical ganciclovir medication at that point and financial problem for systemic medication. She developed maculopathy (mild scotomas from some areas of macula) after an intravitreal injection. After this case, we stopped treating CMV-related anterior uveitis with intravitreal injections of ganciclovir. A patient presented with CMV intermediate uveitis. Ocular examination showed mild unilateral anterior chamber inflammation, diffuse iris atrophy, vitreous

Table 1: Diagnosis of ocular CMV infection in immunocompetent and immunocompromised patients.

Diagnosis	Immunocompetent patients (n, %)	Immunocompromised patients (n,%)		
		HIV	Non-HIV	Total
Anterior segment disease	22 (88%)	0	0	0
Posner Schlossman syndrome (PSS)	14 (56%)	0	0	0
Fuchs heterochromic iridocyclitis	3 (12%)	0	0	0
Endotheliitis	3 (12%)	0	0	0
Combined PSS with endotheliitis	2 (8%)	0	0	0
Posterior segment disease	3 (12%)	14 (100%)	2 (100%)	16 (100%)
Intermediate uveitis	1 (4%)	0	0	0
CMV retinitis	1 (4%)	14 (87.5%)	1 (SLE,6.3%)	15 (93.8%)
Acute retinal necrosis	1 (4%)	0	1 (DLBCL,6.3%)	1 (6.3%)
All	25 (61%)	14	2	16 (39%)

SLE: Systemic lupus erythematosus, CMV: cytomegalovirus, DLBCL: diffuse large B-cell lymphoma

haze and normal retina. Both aqueous and vitreous PCR yielded CMV. He was treated with therapeutic vitrectomy and topical corticosteroids. Inflammation was controlled after treatment without antiviral therapy.

CMV retinitis (n=16) has been found in 14 patients with HIV infection, 1 patient with SLE and 1 immunocompetent patient. Five cases (31.3%) of CMV retinitis received combined intravenous ganciclovir and intravitreal injections of ganciclovir while other 11 cases (68.8%) were treated with only intravitreal injections of ganciclovir. Most patients (n=15, 93.8%) responded well to treatment. The mortality rate of patients with CMV infection in acquire immune deficiency syndrome was 6.3%. CMV related acute retinal necrosis patients was found in 2 cases (1 immunocompetent case, 1 diffuse B cell lymphoma), treated with intravenous ganciclovir injections adjunctive with intravitreal injections of ganciclovir and followed by valganciclovir therapy.

In the immunocompetent group, complications included ocular hypertension in 40% of cases (n=10), glaucoma in 48% of cases (n=12), cataract in 56% of cases (n=14), endothelial cell count loss in 40% of cases (n=10), corneal decompensation in 8% of cases (n=2) and epiretinal membrane in 20% of cases (n=5). No cystoid macular edema was found. Surgical management included cataract surgery in 32% of cases (n=8), glaucoma surgery in 44% of cases (n=11) and keratoplasty in 8% of cases (n=2).

In the immunocompromised group, complications included ocular hypertension in 25% of cases (n=16), cataract in 25% of cases (n=4), rhegmatogenous retinal detachment in 31.3% of cases (n=5) and cystoid macular edema in 6.3% of cases (n=1). No glaucoma was developed. Cataract surgery was performed in 12.5% of cases (n=2).

In both groups, 18 patients received systemic antiviral agents and 16.7% of cases (n=3) developed bone marrow suppression. Onset of bone marrow suppression of 3 cases was 4 weeks, 6 weeks and 30 weeks after valganciclovir initiation.

Discussion

In our study, clinical features of CMV-related ocular diseases were varied with anterior uveitis mostly presented in immunocompetent host and posterior uveitis frequently occurred in immunocompromised host. We do not know the reason why the target site of the virus differed among hosts with various immune statuses.

Regarding CMV related anterior uveitis, there were various clinical presentations, including PSS, FHI, endotheliitis, and combined presentation such as PSS with endotheliitis.[16-22] We hypothesized that the amount of virus in the innoculation site may be the factor to determine the clinical presentation. In PSS, virus may be mostly located in trabecular meshwork. This may be different from FHI which infected site mostly located in iris. Corneal endothelium may be the target site for corneal endotheliitis.[18] From our study, the clinical clues suggesting CMV related anterior uveitis included diffused iris atrophy (most frequent finding) followed by increased intraocular pressure. Additional suggestive signs included coin-shaped lesions, decreased endothelial cell count.[21] Glaucoma was a common complication. Most patients (88%) had increased intraocular pressure with 48% progressed to glaucoma and 44% needed glaucoma surgery to control their intraocular pressure. PSS was the most common clinical presentation in CMV related anterior uveitis. In the past, PSS was considered to be a benign condition.[17] In our study, glaucoma can develop in nearly half of patients. We would like to emphasize that PSS is not always benign. Glaucoma monitoring is essential and the patient can develop blindness in this disease.

In this study, immune recovery uveitis was found in 20% of HIV patients. This is in range of previous records, which are varied between studies, ranging from 1.5-63.3%.[23, 24] This may be because of there is no specific criteria for diagnosis IRU and depend on awareness of the ophthalmologists. The risk of IRU included low CD4+ T cell count and large infected areas of CMV retinitis. The high incidence may be from large area

Table 2: Complications of ocular CMV infection in immunocompetent and immunocompromised patients.

Complications	n	Increased IOP		Need glaucoma surgery	Cataract	Cataract surgery	EDC loss (eyes)	Corneal decompensation	keratoplasty	CME	RRD	ERM	Maculopathy	Optic atrophy	Immune recovery uveitis
		OHT	Glaucoma												
Immunocompetent host															
PSS	14	8	6	10[a]	9	4	4	0	0	0	0	1	1[c]	0	0
FHI	3	1	1	0	0	0	2	0	0	0	0	2	0	0	0
Endotheliitis	2	1	1	0	2	2	3	0	0	0	0	1	0	0	0
Bullous keratopathy	1	0	1	0	0	0	0	1	1	0	0	0	0	0	0
Combined PSS with endotheliitis	2	0	2	1[b]	1	0	1	1	1	0	0	0	0	0	0
Intermediate uveitis	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
CMV retinitis	1	0	1	0	1	1	0	0	0	0	0	1	0	0	0
Acute retinal necrosis	1	0	0	0	1	1	0	0	0	0	1	0	0	1	0
Total	25	10 (40%)	12 (48%)	11 (44%)	14 (56%)	8 (32%)	10 (40%)	2 (8%)	2 (8%)	0	1 (4%)	5 (20%)	1 (4%)	1 (4%)	0
Immunocompromised host															
CMV retinitis	15	1	0	0	2	2	-	0	0	1	5	1	1	5	3 (20%)
Acute retinal necrosis	1	1	0	0	0	0	-	0	0	0	0	0	0	0	0
Total	16	2 (12.5%)	0	0	2 (12.5%)	2 (12.5%)	-	0	0	1 (6.3%)	5 (31.3%)	1 (6.3%)	1 (6.3%)	5 (31.3%)	3

IOP: intraocular pressure, OHT: ocular hypertension, CME: cystoid macular edema, RRD: rhegmatogenous retinal detachment, ERM: epiretinal membrane, PSS: Posner Schlossman syndrome, FHI: Fuchs heterochromic iridocyclitis

Corneal endothelial cell density loss (EDC loss) >20% in unilateral case compare with fellow eye or loss >20% compare with lower margin of normal range of each age group in bilateral cases.

a: Trabeculectomy with mitomycin C 8 patients, combined phacoemulsificatoin with intraocular lens implantation with trabeculectomy with mitomycin C 2 patients

b: Trabeculectomy with mitomycin C

c: Toxic from intravitreal ganciclovir injection

of retinitis and high number of patients who had low CD4+ T cell count. We also believe that the practitioner's awareness is another factor involving the incidence of immune recovery uveitis because IRU can present with mild or severe inflammation. Signs of immune recovery uveitis included iritis, mild to severe vitritis, macular edema, epiretinal membrane formation, neovascularization of the retina or optic disc and papillitis.[24]

CMV-related ocular diseases vary in severity, from spontaneously resolved to severe visual impairment and many complications can occur both from the diseases themselves and from the treatments.[25, 26] The complications found in our study are ocular hypertension, glaucoma, cataract, endothelial cell loss, corneal decompensation, cystoid macular edema, retinal detachment, epiretinal membrane, maculopathy and optic neuropathy. Leukopenia from systemic anti-CMV medication can occur in weeks or years. Blood monitoring is essential during systemic therapy.

The important limitations of our study are the incomplete information in the medical records and small number of patients included in the study.

Conclusion

Cytomegalovirus can infect both immunocompetent and immunocompromised host with variety of clinical features. Anterior uveitis was common in immunocompetent cases while retinitis was common in immunocompromised patients.

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Visual acuity improvement in bilateral corneal scars following the use of rigid gas permeable contact lens : a case report

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Background: Corneal scarring often results in impaired visual acuity due to irregular astigmatism inadequately corrected with spectacles. Rigid gas permeable (RGP) contact lens (CL) offers a practical, less invasive, and less expensive alternative to surgery in negating the irregular astigmatism of eyes with corneal scars.

Case description: A 40-year old female presented with blurred vision of both eyes since a year ago with a history of recurrent redness on both eyes. Her visual acuity was 6/30 on the right eye and 6/15 on the left eye uncorrected with pinhole. There were multiple scars with vascularization on bilateral corneas without active signs of inflammation. Fitting for RGP CL was performed. Keratometry readings were obtained with distorted mires. The corneal topography showed irregular patterns. A trial was performed using a tisilfocon A lens with base curve 8.40 mm for the right eye and 7.60 mm for the left eye, power S-4.00D and diameter 9.20 mm. Over-refraction with the trial lens could determine the final power and the final visual acuity achieved with the RGP CLs was 6/15 on the right eye and 6/7.5 on the left eye.

Conclusion: With proper fitting, RGP CL can be a treatment option in improving the visual acuity for patients with corneal scars, thus helping to further delay surgical treatment and improve patient's quality of life.

Conflicts of Interest: The authors have no financial interest in the subject matter of this case report.

Keywords: Rigid gas permeable contact lens, corneal scars, irregular astigmatism, irregular cornea, contact lens fitting

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Introduction

Corneal scarring often results in impaired visual acuity by light scatter due to an irregular corneal surface. Such patients often have co-existing high irregular astigmatism which cannot be adequately corrected with spectacles in most cases. Global estimates suggest that corneal opacities cause accounts for 4% of total blindness in 2010.[1] Based on 2013 Basic Health Research the prevalence of corneal opacities in Indonesia is 5,5%.[2]

One of the non-surgical management for improving visual acuity is contact lens. Rigid gas permeable (RGP) contact lens (CL) helps in negating the irregular astigmatism due to corneal scarring, by providing a smooth refracting surface.[3] Prior studies have reported successful use of RGP

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CL in improving vision in cases of corneal opacities.[3-10]

This is a case of bilateral corneal scars which causes irregular refractive surface and opacities in the stroma that could not be fully corrected with spectacles, thus RGP CLs were chosen as management. This report aims to demonstrate that RGP CLs with proper fitting can be an alternative option for patients with corneal scars in improving the visual acuity.

Case Discription

A 40-year old female came to the hospital with a chief complaint of blurred vision of both eyes since a year earlier. There was a history of recurrent redness on both eyes, sometimes unilateral, with no discharge since two years ago. She instilled an eyedrops containing combination of steroid and antibiotics and the redness subsided but the blurred vision remained. There were whitish appearances on both eyes over time. There was no history of chronic cough, skin rash, joint pain nor hair loss. There was no history of wearing contact lens nor spectacles. There was no history of ocular trauma nor systemic disease. She denied any similar condition in her family.

Upon ophthalmological examination, the patient's initial visual acuity (VA) was 6/30 on the right eye and 6/15 on the left eye uncorrected with pinhole. The potential acuity measurements examined by retinometry were 0.8 (equivalent to 6/7.5) and 0.9 (equivalent to 6/6.6). There were translucent fibrovascular tissue on both eyes. The fibrovascular tissue on the left eye was thicker than the right, but both only extend from the lateral canthus to the limbus. There were also multiple epithelial and stromal scars with vascularization, located centrally and paracentrally on the bilateral corneas, but without active signs of inflammation on the anterior segment. The scars rae quite prominent, especially in the left eye, so hat the iris detail can not be visualized well. The pupils of both eyes were round, central, with positive light reflex. The posterior segment of both eyes was normal. She was diagnosed with multiple corneal scars of both eyes. The etiological differential diagnosis includes infectious keratitis dan immune related keratitis. And she was then referred for RGP CLs.

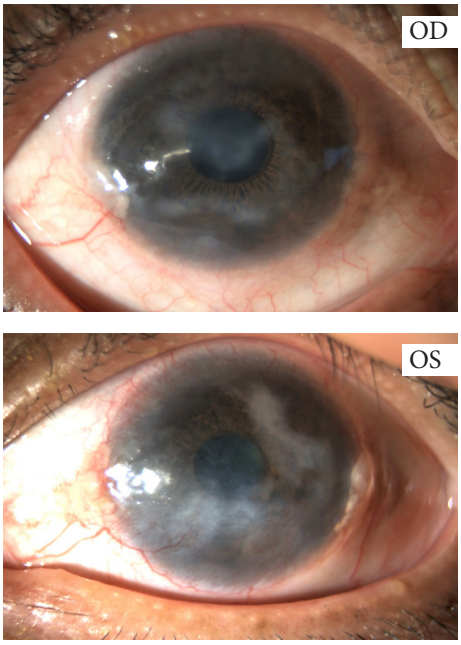

Figure 1: The profiles of the cornea of both eyes, as seen from the anterior with the slit lamp. There are significant multiple scars with neovascularization.

Although thew mires during manual keratometry were formed with some distortions, the corneal curves could be determined approximately 40.75 D (8.7 mm) at 0° for horizontal curvature and 46.75 D (7.2 mm) at 90° for vertical curvature in the right eye, while in the left eye the keratometry readings were 43.00 D (7.85 mm) at 5° for horizontal curvature and 51.00 D (6.50 mm) at 95° for vertical curvature. The corneal topography of the right eye showed that the radius of horizontal

curvature was 8.97 mm and the radius of vertical curvature was 6.98 mm, while the corneal topography of the left eye showed that the radius of horizontal curvature was 7.64 mm and the radius of vertical curvature was 6.79 mm.

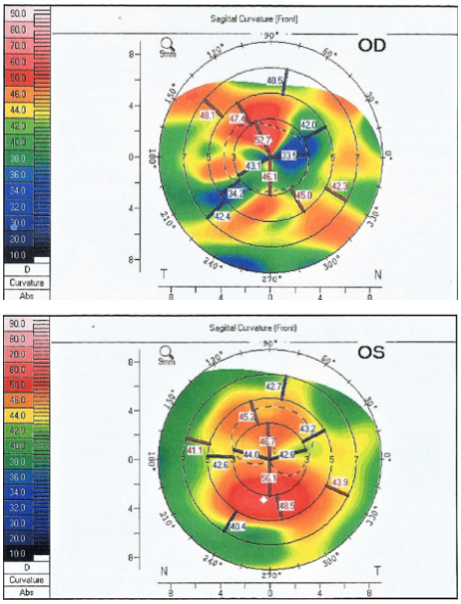

Figure 2: The corneal topography of both eyes showed irregular patterns.

Trial fitting for RGP CL was then performed tisilfocon A (Menicon Z α) lens with base curve 8.40 mm for the right eye and 7.60 mm for the left eye, power spherical -4.00 Diopter and diameter 9.20 mm for both eyes. There was a temporal/inferior CL decentration on the right eye, but the pupil was still covered by the lens. While on the left eye, there was an inferior decentration approximately 1 mm. The movement on blink was adequate, although there was a rocking movement of the CL in the right eye. Instillation of the fluorescein eyedrops and examination with cobalt blue light showed irregular patterns on both eyes but with relatively good central alignment. Overall, it was an acceptable fitting.

The overrefraction with the trial lens revealed residual errors of spherical +6.00D in the right eye and of spherical +4.00D in the left eye while the best corrected visual acuity (BCVA) was 6/15 on the right eye and 6/7.5 on the left eye. Menicon Z α were then ordered for her with parameters as follow: base curve 8.40 mm with power +2.50D and diameter 9.20 mm for the right eye and base curve 7.60 mm with power +0.25D and dimeter 9.20 mm for the left eye.

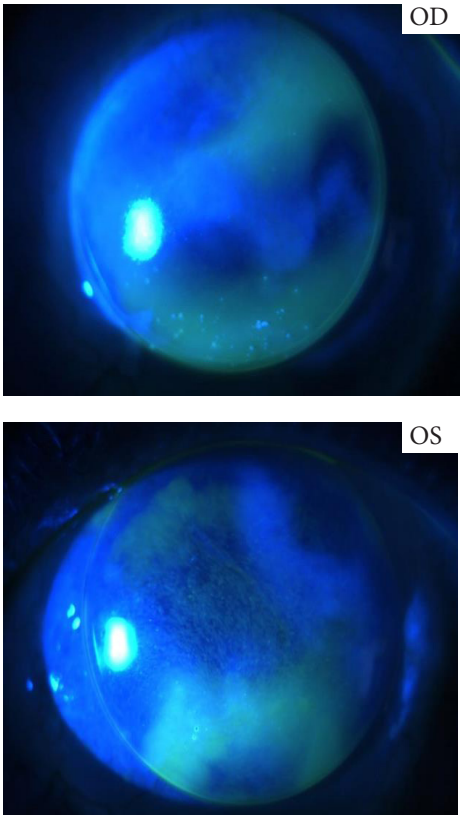

Figure 3: Irregular patterns on both eyes after fluorescein application with the RGP CLs.

Patient received ordered RGP at the next visit and was educated on how to wear and take care of the CLs. The patient was educated how to wear and take care the CLs. The visual acuity with the RGP CLs was measured and there was similar visual acuity as measured at the trial. A week

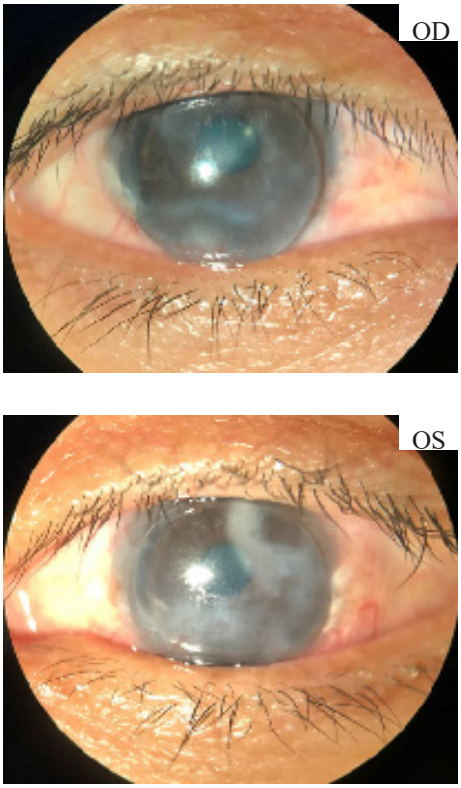

Figure 4: The patient wearing the RGP CLs, some decentrations were shown but with adequate pupil coverage.

after wearing the CLs, the patient noted significant subjective visual improvement with the CLs with no complaints about the CLs wear. The patient reported that overall comfort was also improving, as she was able to wear the lenses every day for a maximum of 12 hours a day.

Discussion

Corneal opacities occur when altered stromal keratocytes either fail to produce certain chemical factors after infection, trauma, or surgery or form underlying disease or dystrophy. New collagen fibers become disorganized, scatter light, and result in a non-transparent scar.[11] Corneal opacity causes irregular astigmatism due to irregularities of the corneal surface.

Irregular astigmatism occurs when the orientation of the principal meridians changes from one point to another across the pupil, or when the amount of astigmatism changes from one point to another. Irregular astigmatism may also be defined as an astigmatism state not correctable by a spherocylindrical spectacle lens. A comprehensive definition by Duke Elder states that irregular astigmatism is a refractive state in which refraction in different meridians conforms to no geometrical plan and the refracted rays have no planes of symmetry. Irregular astigmatism has been considered an uncommon refractive error. The astigmatism compensation with spectacle lenses is possible if the primary meridians are perpendicular because ophthalmic astigmatic lenses can only correct orthogonal astigmatisms.[12]

It is difficult to correct irregular with standard spectacles, since ophthalmic astigmatic lenses correct only orthogonal astigmatism where primary meridians are perpendicular.[12] Therefore, contact lens could be a choice to improve visual acuity in cases with irregular astigmatism.[6,12] Rigid gas permeable contact lens may be the lens of choice, since it provides good visual acuity, corrects high degrees of regular and irregular astigmatism, has high oxygen permeability, and, in comparison with soft contact lenses, carries a lower risk of microbial keratitis and corneal neovascularization.[13]

Since the refractive index of tears and cornea is similar, the tear lens can neutralize more than 90% of the regular and irregular corneal astigmatism. The tear lens is an additional lens in which the anterior curvature radius is determined by the back RGP lens radius, and the posterior radius coincides with the anterior corneal curvature. Therefore, the difference in the power of the steepest and flattest corneal meridians is neutralized by the RGP CLs. It masks the underlying irregular cornea and

provides a new refractive surface.[14]

In this case, the patient came with the chief complain of blurred vision in both eyes, with a history of recurrent keratitis. Corneal scars on both eyes was found from slit lamp examination. The right eye initial visual acuity was 6/30 and the left eye was 6/15, uncorrected with pinhole. The manual keratometry showed +6.00D at 90° astigmatism on the right eye and +8.00 at 90° astigmatism on the left eye, both with distorted mires. Therefore, this was a case of high irregular astigmatism due to corneal scars. Since RGP CLs offers several advantages, such as superior vision due to correction of corneal cylinder and greater contrast sensitivity, long-term comfort after adaptation, durability, and ease of care, and higher oxygen permeability values, we decided to manage this patient's condition with RGP CLs. [13,15]

However, extra care must be taken into consideration before deciding to treat this patient with contact lens since it was suspected that the corneal opacities were caused by infection. It must be assured that there was no active inflammation or infection before CL fitting. Precise RGP fitting is important to optimize the refractive correction. There are some individualized parameters that need to be determined before the fitting, including base curve radius, overall diameter, lens material and design, lens power, and center thickness.

From the patient's keratometry readings, there were high astigmatism. the base curves selected for both eyes were 0.3 mm steeper than the flattest K. An "on K" BCR fitted on a highly astigmatic cornea will not only provide very little corneal alignment and subsequent decentration, but the resulting areas of bearing and excessive clearance may also result in lens "rocking" on the cornea with the blink, discomfort caused by an increase in edge contact with the upper lid, and corneal desiccation.[15] The manual keratometry readings with distorted mires could not show an irregular astigmatism in this patient, so corneal topography is needed since it is better in measuring irregular astigmatism more accurately. With corneal topography, an asymmetry between the superior and inferior or nasal and temporal halves of the cornea may also be identified.[12] In this patient, the corneal topography of both eyes showed irregular patterns.

The lens design chosen for this patient was an aspheric lens, which provides better centration on irregular astigmatic corneas. Aspheric designs may follow the corneal shape closely, lessening areas of contact between the lens and peripheral cornea, thus enhancing tear fluid exchange and corneal wettability. Furthermore, aspheric lens designs can minimize lid–lens interaction, thereby decreasing discomfort and interference with blinking habits.[15] The diameter of the lens chosen for fitting was 9.20 mm, which was the only diameter available in the trial lens kit and an average for normal corneal size.[3] The power of the lenses was determined by over-refraction since the manifest refraction could not be obtained in this case. The final power was the sum of the trial lens power and the over-refraction. Measuring the over-refraction during a rigid lens trial fitting not only helps to determine the final lens power but also gives an indication of whether the optimum fit has been obtained.[16]

The next step was to see the centration of the trial lenses. For an irregular cornea, the fluorescein pattern nearly always shows the irregularity of the corneal surface.[16] In this case, the patterns and the movement when blinking were consistent with the corneal topography profiles. The fitting is decided according to visual improvement.

In this case, RGP CL that was chosen for fitting and subsequently for use was a tisilfocon A material which has the highest oxygen permeability (Dk) value of 163 barrers.[15] This lens material is a

polymer composed of siloxanylstyrene, fluoromethacrylate, and benzotriazol UV absorber. The hyperpermeable material makes it well suited for diseased eyes that require adequate oxygenation for successful contact lens wear.

From the slit lamp examination, the corneal opacities are different between the two eyes. The scars in the right eye are more diffuse and superficial, while in the left eye they are denser but located paracentrally. The fine, diffuse regular opacity involving the pupillary axis more commonly interferes with vision than the localized, dense cicatricial lesion outside of the visual axis. These opacities irregularly refract light and blur the retinal image. In cases of deep lesions that produce scars outside the visual axis, visual rehabilitation is more feasible than for scars localized in the optical zone.[18] Therefore, the visual acuity after the correction with the CLs was better on the left eye than on the right eye.

The improvement of the patient's visual acuity with contact lens wear far exceeded the straylight. Using the trial lenses, the BCVA improved from 6/30 to 6/15 on the right eye and from 6/15 to 6/7.5 on the left eye. Although visual acuity of 6/6 was not achieved, the patient was satisfied with the improvement. RGP CLs remain a clinically useful treatment option in most patients with corneal scars.

Conclusion

With proper fitting, rigid gas permeable contact lens can be a treatment option in improving the visual acuity for patients with corneal scars, thus helping to further delay surgical treatment and improve patient's quality of life. Nonetheless, careful evaluation of the eye condition with corneal scars before deciding to treat with contact lens is necessary to assure that there is neither active infection nor inflammation.

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Alor setar experience: surgical outcomes of macular hole surgery with folding method

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Purpose: To review the surgical outcomes of macular hole surgery with internal limiting membrane (ILM) folding method in Hospital Sultanah Bahiyah (HSB), Alor Setar.
Method: A retrospective study reviewing the functional and anatomical outcomes of macular hole surgery with ILM folding method for all related cases in HSB during the period between January 2013 to December 2018.
Results: Thirty-seven patients with purely full-thickness macular hole who underwent ILM folding method surgery were included in the study, with 21 females and 16 males. Ages ranged between 51-74 years. We observed the outcomes of macular hole surgery using folding method based on visual improvement and macular hole closure at 6-weeks and 6-months post-surgery. All surgeries were performed by a single vitreo-retinal surgeon in HSB. Following macular hole surgery using folding method, 31 cases (83.8%) and thirty-three cases (89.2%) showed visual improvement by two or more lines at 6-weeks and 6-months post-surgery, respectively. Hole closure was achieved in all cases (100%) of macular hole surgery using the folding method at 6 weeks and 6 months post-surgery.
Conclusion: In conclusion, surgical outcomes of macular hole surgery using ILM folding method in Alor Setar showed 100% anatomical success and majority of cases showed improvement in visual acuity by 2-or-more line at 6-months post-surgery. Besides surgical techniques, macular hole surgical success is also attributed by size of macular hole.
Keywords: macular hole surgery, folding method, surgical outcome
Conflict of interest statement: We declare that we have no conflict of interest
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Introduction

Idiopathic macular hole is one of the causes of significant reduction in visual acuity particularly in women in the seventh decade of life.[1] Visual disturbance is believed to be due to dehiscence at the umbo, loss of retinal tissue in the hole and detachment of the neurosensory retina surrounding the hole.[2] Gass has suggested that macular holes are the result of a dehiscence of the retina at the macula, and that this dehiscence is due to tractional forces on the macula by the prefoveal vitreous cortex, and by epiretinal membranes, especially in a tangential manner.[3]

Kelly and Wendell reported the first successful closure of a series of macular

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holes by pars plana vitrectomy and gas tamponade in 1991.[4] In the past literature and studies, rate of successful macular hole closure is higher in 'newer' macular holes as compared to long-standing macular holes.[5] Conventionally, most macular hole surgery involves 'peeling' method where vitrectomy, peeling of the internal limiting membrane (ILM) and gas tamponade. In 2010, a slightly newer technique was introduced to address larger and chronic macular holes; the inverted ILM flap or also known as 'folding' method in our study, where the surgeon leaves a piece of ILM attached to the edge of the hole, flattened and subsequently folded over the hole in an inverted manner to leave the hole covered after fluid-gas exchange.[6] It is believed that the flap serves as a scaffold to induce and support glial cell proliferation, which founded the hole-closure process. [6]

Objective

To review the surgical outcomes of macular hole surgery with internal limiting membrane (ILM) folding method in Hospital Sultanah Bahiyah (HSB), Alor Setar, Kedah, Malaysia.

Method

A retrospective study reviewing the functional and anatomical outcomes of macular hole surgery with ILM folding method for all related cases in HSB during the period between January 2013 to December 2018. Data were collected retrospectively from patients' case notes and inserted into a predetermined proforma on Microsoft Excel. Patient demographic data, diagnosis, underlying illness, pre- and post-operative vision and Optical Coherence Tomography (OCT) macular findings pre- and post-operatively were recorded. Those with previous or known retinal diseases limiting visual acuity such as retinal detachment, any types of retinopathy or posterior uveitis, and previous vitrectomy ILM folding method surgery with C3F8 gas tamponade were included in the study, with 21 females and 16 males. Ages ranged between 51-74 years.

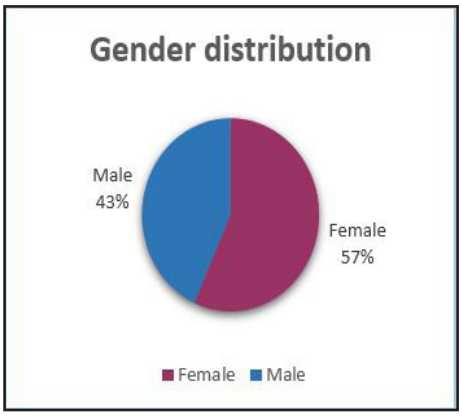

Figure 1: Pie chart depicting the gender distribution of patients who underwent macular hole surgery ILM folding method in HSB between the period of January 2013 to December 2018.

Based on Gass' classification of macular hole, 18 (48.6%) were stage 3, 17 (45.9%) were of stage 2 macular hole and only 2 cases were of stage 4. We observed the outcomes of macular hole surgery using folding method based on visual improvement and macular hole closure at 6-weeks and 6-months post-surgery. Surgical outcomes were evaluated based on anatomical and functional parameters. Case were deemed an anatomic success if the macular hole closes as evidenced by the OCT imaging done post-operatively. Functional success is defined as an improvement in visual acuity by 2 lines or more on Snellen projection following macular hole surgery. All surgeries were performed by a single vitreo-retinal surgeon in HSB, which followed the same post-operative care and positioning as guidelined. Following macular hole surgery using folding method, 31 cases (83.8%) and thirty-three cases (89.2%) showed visual improvement by

two or more lines at 6-weeks and 6-months post-surgery, respectively (Figure 2 and Figure 3). Remaining 4 cases which had no improvement in visual acuity (VA) were of stage 3 (2 cases) and stage 4 (2 cases), all of which had no drop in VA at 6-months post-surgery.

Post-operative visual acuity ranged from 6/9 to counting fingers on standardised Snellen projection. Best visual results were seen in those eyes with stage 2 holes, 45.9% (17 eyes) of these eyes achieved final best corrected visual acuity of 6/18 or better.

Out of the 100% anatomically-success eyes, 4 (10.8%) showed functional failure, in which post-operative visual acuity remained static or improved by only a single line on Snellen chart, as compared to pre-operative vision. No patient demonstrated deterioration in visual acuity following macular hole surgery in this audit.

Lens opacities have progressed to cause significant cataracts post gas tamponade in 26 patients which requires cataract removal to date. On average, cataract were detected between 6-months to 15 months post vitrectomy surgery. No other immediate visual-threatening complications seen in all patients included in the study.

Hole closure was achieved in all cases (100%) of macular hole surgery using the folding method at 6 weeks (Figure 2 - above) and 6 months post-surgery (Figure 3 - below).

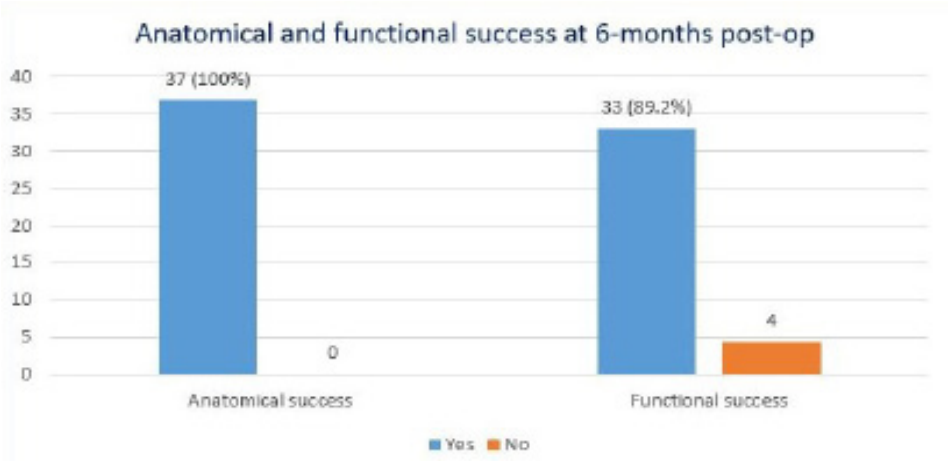

Table 1: the outcomes of macular hole surgery using folding method

Visual outcome at 6 months post-surgery	Folding method
No improvement	1 (2.7%)
1 line	3 (8.1%)
2 lines or more	33 (89.2%)

Discussion

The main goal of surgical therapy for macular hole is for visual improvement through closure of the hole and flattening of the cuff of subretinal fluid surrounding the hole.[2] Besides, the anatomical success of macular hole surgery, the visual restoration is highly dependent on the preservation of surrounding retinal tissues which contributes to emergence of new surgical techniques. The macular hole surgery performed in our centre is similar that of described by Kelly and Wendel[4] involving pars plana vitrectomy, gas tamponade and post-operative posturing. Folding method involves trimming of the macular hole edges and subsequently flattening it rather than the normal membrane peeling before subsequently folded over the hole in an inverted manner to cover the hole after fluid-gas exchange (figure 4).

Others have proposed techniques such as aggressive peeling of very fine epiretinal membranes (ERM) and drainage of subretinal fluid through the macular hole. Minihan et al 1997[2] noted that fine ERM at macula, which usually contracted post-operatively, does not interfere with vision or increased risk of traction. They concluded that it is therefore possible to achieve high anatomic success rate despite avoiding aggressive peeling of fine ERMs or of the ILM which may cause nerve fibre layer haemorrhages.[2] Glaser et al 1992 projected a high anatomic success rate achievement following macular hole surgery without foveal manipulation.[8]

In addition, there are several factors needed to be considered by ophthalmic surgeons which determine the potential outcome of macular hole surgery and ethically compulsory to be included in the risk-benefit analysis discussion with patients pre-operatively. These include the chronicity of defect, size and stage of the hole, status of surrounding retinal tissues and pre-operative visual acuity. Ullrich et al[9] demonstrated the role of pre-operative measurement of macular hole size with OCT in providing predictive value for visual and

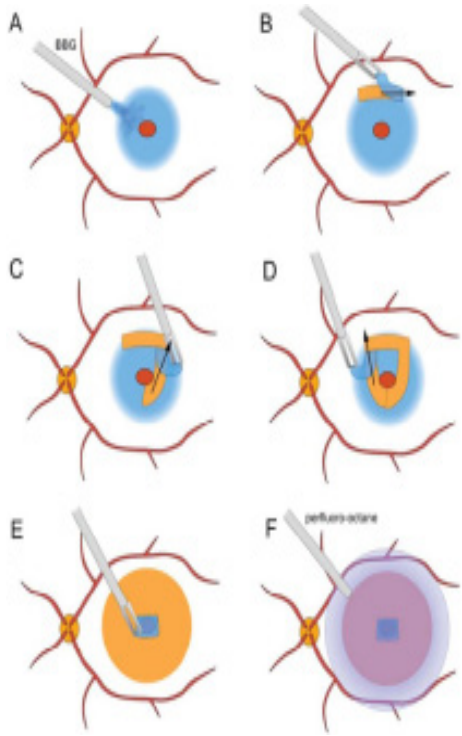

Figure 4: Diagrammatic representation of surgical technique to make an ILM-folding (adopted from Shin et al 2014[7])

anatomical success of macular hole surgery. The study also showed the superiority of hole base diameter (measured using OCT machine) as a prognostic tool as compared to slit lamp examination which is subjective to examiners involved and hence unable to reflect the real size of the retinal lesion. Similar results published by Freeman et al[10] in 1997 also suggested that a macular hole with a small diameter was associated with better functional outcome as it might indicates better preserved macula, similar to results obtained in our study where all 4 cases with no improvement in VA were of Gass' stage 3 and 4 macular hole (size >400μm). Ullrich and co-workers added that no correlation found between the duration of symptoms and the diameters measured.[9]

In 1994, Ryan et al[11] evaluated the visual prognosis following macular hole surgery in 'recent' and 'old' holes. Subjects were considered to be having 'recent' holes if they were symptomatic for less than 6 months whereas patients with symptoms lasting more than 6 months were classified as 'old' holes. They concluded that recent macular holes demonstrated better visual outcomes than that of older holes and considered beneficial by most patients in the study.[9] In our study, data is not available on the chronicity of the hole due to difficulty for patients to identify the exact time onset of symptoms and most of our patients presented rather late (Gass' stage 2 and above).

There is evidence suggesting that longer duration of intraocular gas tamponade may produces better outcome of macular hole surgery.[12] In our centre, we enforce to our patients regarding the importance of posturing post-operatively for higher success outcomes. We provided patients with ample information on posturing duration and techniques, verbally as well as information leaflet given following surgery. Posturing remains a troublesome and unpleasant requirement for patients and we believe that it does contributes towards desirable surgical outcomes.

Limitations of the audit and its implications

The smallest macular holes done using folding method in our centre was 323μm, which falls into Gass' stage 2 macular hole. In the future, we would like to aid our cases-method selection by following international guideline in which macular hole is considered to be large if it is more than 400μm (Gass' stage 3 and 4). Besides, some macular hole stages were not properly documented, which limit our controlling power in auditing our cases. In the future, proper documentation of macular hole stages will be useful for future audits.

This audit helped to change our practice as it helped to construct new guideline for us in surgical technique selection. We have concluded that folding method will be the method of choice for all chronic macular holes (more than 1 year), stage 4 and large holes (size more than 400μm). We have also composed a new template clerking for all macular hole cases to aid us in decision-making and managing patient better. These efforts will hopefully be able to optimize our management and patient care services in the near future and subsequently offer successful outcomes in restoring vision.

Conclusion

In conclusion, surgical outcomes of macular hole surgery using ILM folding method in Alor Setar showed 100% anatomical closure and majority of cases demonstrated improvement in visual acuity by 2-or-more line at 6-months post surgery. Besides surgical techniques, macular hole surgical success is also attributed by size of macular hole, as evidenced in our study data where all Gass' stage 2 macular hole achieved anatomical hole closure and functional success.

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Comparison of intraocular lens power calculation formulas in primary angle closure glaucoma

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Objective: To compare the accuracy of intraocular lens (IOL) power calculation formulas in primary angle closure glaucoma (PACG) eyes. All the formulations in this study are common and widely used; SRK/T, Hoffer Q, Holladay I and Haigis.
Design: Retrospective chart review
Methods: Data collection was performed through the OPD cards of PACG patients who already had uneventful cataract surgery with monofocal IOL by a single surgeon. All the patients had pre-operative data collection of axial length (AL), anterior chamber depth (ACD), keratometry, and predicted refractive outcomes using SRK/T, Hoffer Q, Holladay I and Haigis by IOL Master (Carl Zeiss version 5) biometry. Post-operative data was also collected. Analysis of the accuracy of all formulas was done by comparison of the predicted refractive outcomes and the measured refractive outcomes using the mean error (ME) and mean error squared (MES). MES was calculated to account for postoperative refractive errors with positive and negative values neutralizing one another in the resulting mean error.
Results: The Hoffer Q formula produced the lowest ME (0.009±0.54 D), but not the MES (0.303 D) Whilst the most accurate formula with the least random error (MES=0.216 D) is SRK/T with also low ME (0.083±0.45 D). The Haigis formula produced the highest MES (0.323 D) this inaccuracy of the Haigis formula may be caused by biometric data (using ACD). However, there is no significant difference between all 4 formulas (within limits of a small sample size). AL is the most weighted variable with significant effect to the predicted refractive error (*P*=0.029). All four formulas have positive ME representing more hyperopic result than intended.
Conclusion: The most accurate formula in this study is SRK/T. Haigis was the least accurate formula, potentially attributed to postoperative ACD changes. There is no significant difference between all 4 commonly used formulas.
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Introduction

We do know that one of the most important factors for precise vision is accurate intraocular lens (IOL) power calculation that mostly depends on the IOL calculation formula. In 2011, Aristodemou P. et al.[1] concluded that Hoffer Q was the most accurate formula in eyes with short Axial length (AL) of 20.00-20.49mm, Hoffer Q and Holladay I were also accurate in eyes with AL 21.00-21.49mm and all modern IOL calculation formulas perform well over the normal AL range.

However, most of the angle closure glaucoma eyes have shorter AL and

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shallower anterior chamber depth (ACD) than normal eyes and these biometric data also change after cataract surgery. Notably, an increase in ACD and AL after cataract surgery from the studies of Nonaka A. et al. and Francis BA. et al. [2,3]

In 2009, Kang SY. et al.[4] summarized that after using the SRK-II formula, angle closure eyes having remaining refractive errors greater than 0.5D was 50%, that is significant when compared to normal eyes (26.67%).

In 2011, Jongsoo Joo. et al.[5] completed a retrospective study comparing the accuracy of IOL Power Calculation Formulas in Primary Angle Closure Glaucoma (PACG) using Hoffer Q, SRK/T and Haigis. The study showed that Haigis is the least accurate formula and Hoffer Q is the most accurate formula when compared to the postoperative refractive error between normal eyes and PACG eyes.

In our study, we aim to compare the accuracy between SRK/T, Hoffer Q, Holladay I and Haigis in PACG eyes that underwent cataract surgery (Phacoemulsification with monofocal intraocular lens) by only one surgeon in order to decrease the confounding factor from surgical induced astigmatism (SIA).

Materials and Methods

Retrospective data collection was performed through the OPD cards of 50 PACG eyes who already had uneventful cataract surgery from 2015 to 2017 in Thammasat hospital. All of the patients were diagnosed as primary angle-closure glaucoma by glaucoma specialists in Thammasat glaucoma clinic and did not have any other ocular diseases or previous ocular surgeries.

Preoperative measurement was performed with IOL Master optical biometer ver. 5 (Carl-Zeiss, Jena, Germany) with Signal to Noise ratio (SNR) more than 10 in all 50 eyes. These biometric data were used to compare with the automated keratometry result of corneal power. If the biometric data from IOL master was not closely related with the data from automated keratometry (> 10% error) then that eye will be excluded from the data collection.

All the PACG patients that underwent uneventful cataract surgery under topical anesthesia using monofocal IOL in the capsular bag (iSert250, SN60WF) by a single surgeon, Dr.Anuwat Prutthipongsit (glaucoma specialist) in order to reduce the effect of surgical induced astigmatism (SIA). The choice of IOL power was based on target refractive outcome (least minus refractive error) on all 4 formulas.

One month after cataract surgery was performed, refractive outcome was measured by an auto-refractometer (Carl Zeiss Meditech AG Goeschwitzer Strasse 51-52 07745 Jena, Germany) and this data was collected for analysis using STATA ver.14.2. The level of clinically significance was set at 0.05 to determine the difference between all 4 formulas using mean error (ME) and mean error squared (MES).

Results

Preoperative data of 50 PACG eyes was shown in Figure 1. Most of the patients were female and mean age was 67.76±9.09 years. Preoperative best-corrected visual acuity (BCVA) was 0.1508±0.2 in logMAR (about 20/28 in Snellen). Preoperative axial length (AL) and anterior chamber depth (ACD) was 22.64±0.86 mm. and 2.67±0.33 mm. respectively. Most of the IOL model were HOYA iSert 250 (N=40) and the rest were AcrySof IQ SN60WF (N=10).

Discussion

In our study, Hoffer Q produced the lowest ME (0.009±0.54D), but not the MES (0.303 D) (Figure 3). This result can be explained from the negative postoperative refractive error (myopia) and the positive postoperative refractive error (hyperopic)

Baseline characteristics	Distribution (N = 50)
Sex	Male = 13 Female = 37
Age	67.76 ± 9.09 (52-85)
IOL model	Isert250 = 40 SN60WF = 10
Pre-op BCVA (logMAR)	0.1508 ± 0.2 (0-0.69)
Pre-op IOP	17.1 ± 0.86 (10-30)
AL	22.64 ± 0.86 (21.11-24.53)
ACD	2.67 ± 0.33 (2.22-3.31)

Figure 1: Preoperative data in PACG patients.

IOL=intraocular lens; IOP=intraocular pressure; BCVA= best-corrected visual acuity; AL= axial length; ACD=anterior chamber depth.

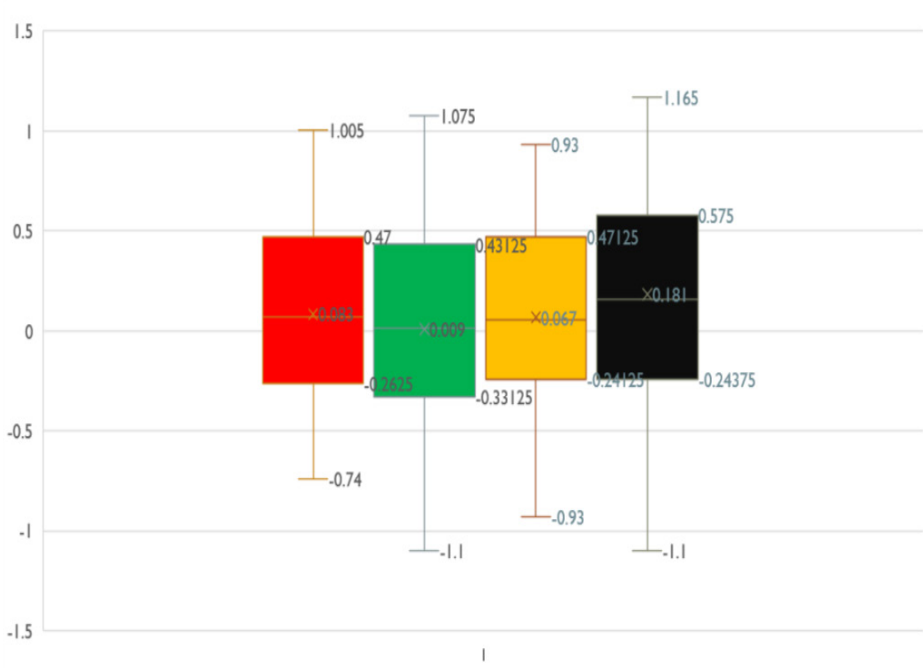

Figure 2: Mean Error (ME) in 4 formulas

Figure 2 shows Mean Error (postoperative refraction - target refraction) of each formula. Red represents SRK/T, Green represents Hoffer Q, Yellow represents Holladay I and Black represents Haigis

Formulas	MeanError (ME/D.)	MeanErrorSquare (MES/D.)
SRK/T	0.083±0.45	0.216
HofferQ	0.009±0.54	0.303
Holladayl	0.067±0.48	0.238
Haigis	0.181±0.53	0.323

Figure 3: Comparing the mean error (ME) and mean error square (MES) in 4 formulas

All 4 formulas produced positive ME, which meant more hyperopic result than intended. MES in Figure 3 was used in order to evaluate all of the negative (myopic) and positive (hyperopic) refractive error that could be neutralized by each other in ME.

Figure 4.1-4.4: Comparing predicted refractive error of 4 formulas with measured refractive error.

X-axis represents measured refractive error and Y-axis represents predicted refractive error in each formula.

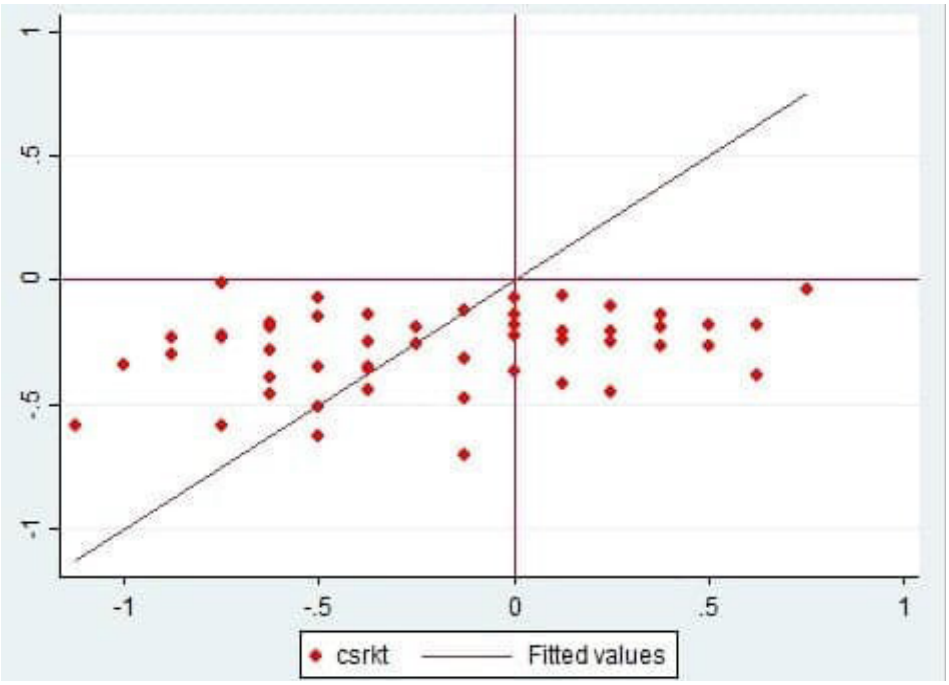

Figure 4.1: SRK/T formula

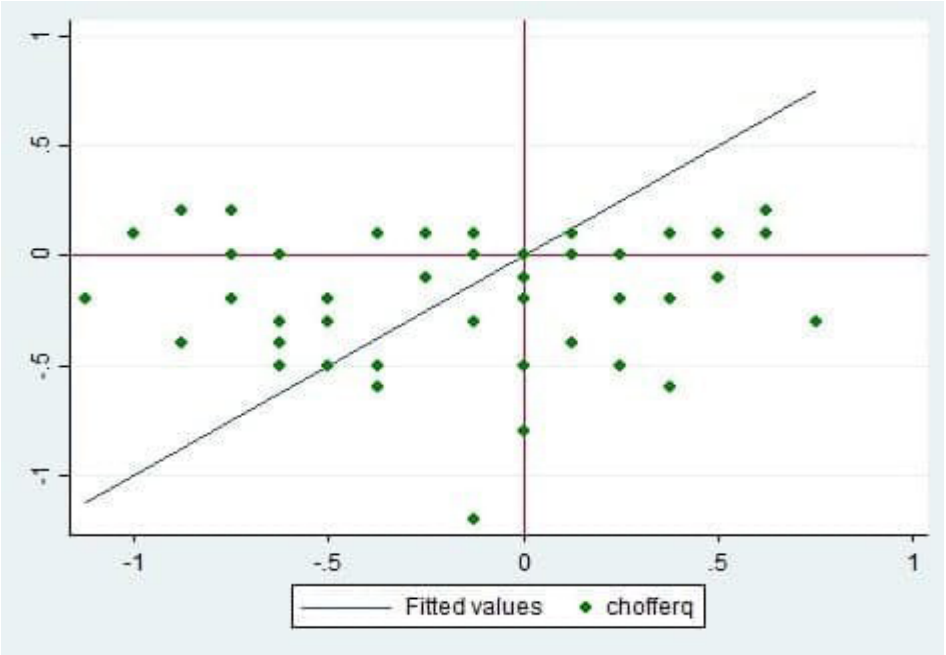

Figure 4.2: Hoffer Q formula

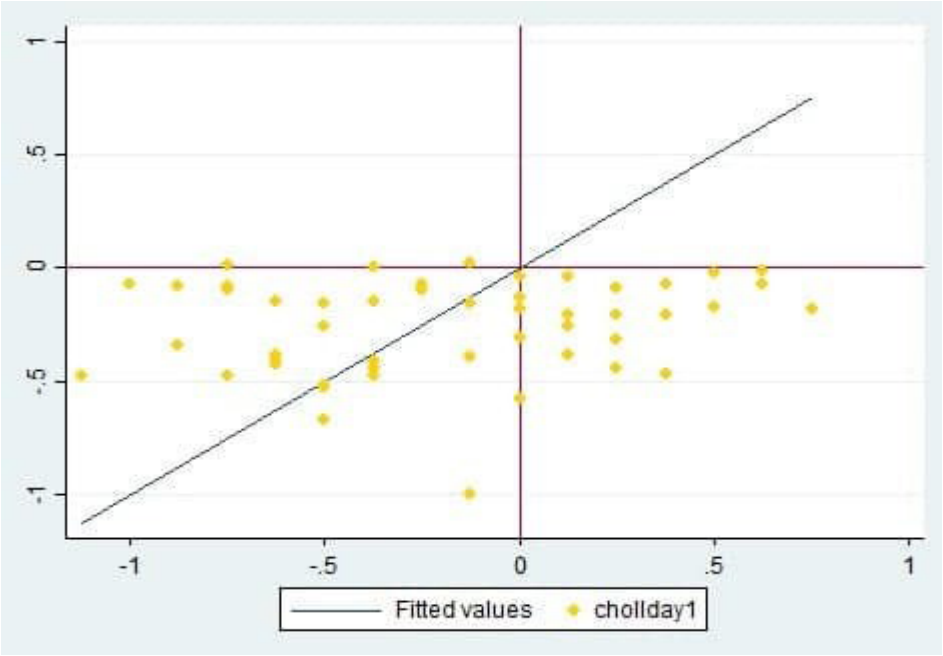

Figure 4.3: Holladay I formula

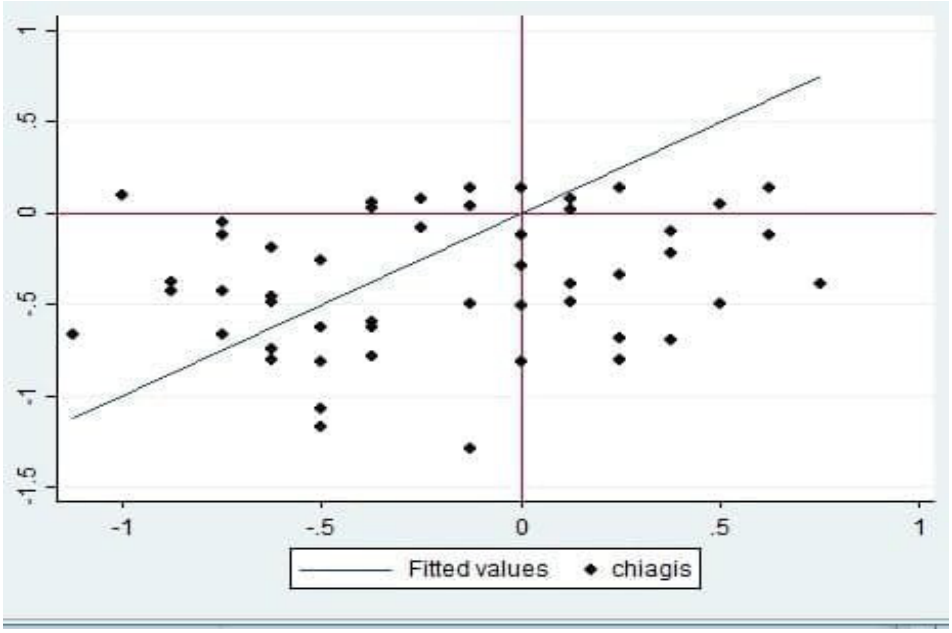

Figure 4.4: Haigis formula

Figure 5.1-5.4: Comparing inaccuracy in predicted refractive error of 4 formulas with measured refractive error

X-axis represents Mean Error (ME) and Y-axis represents predicted refractive error in each formula.

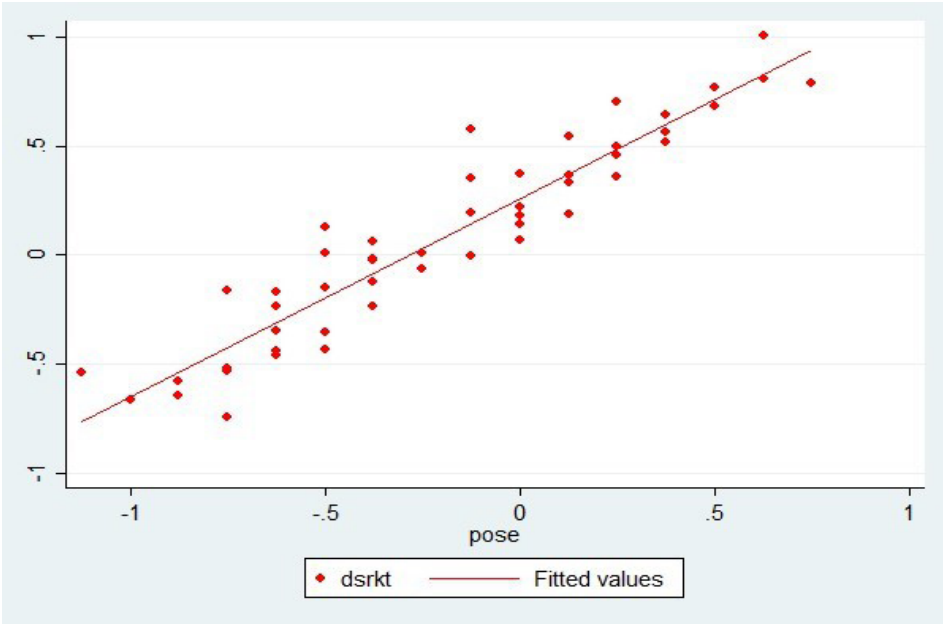

Figure 5.1: SRK/T formula

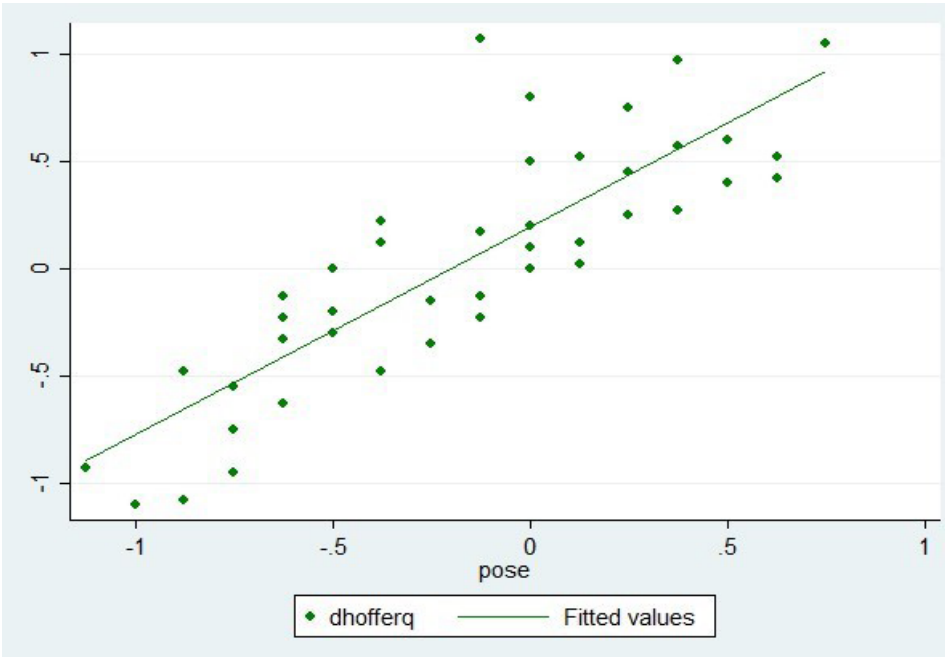

Figure 5.2: Hoffer Q formula

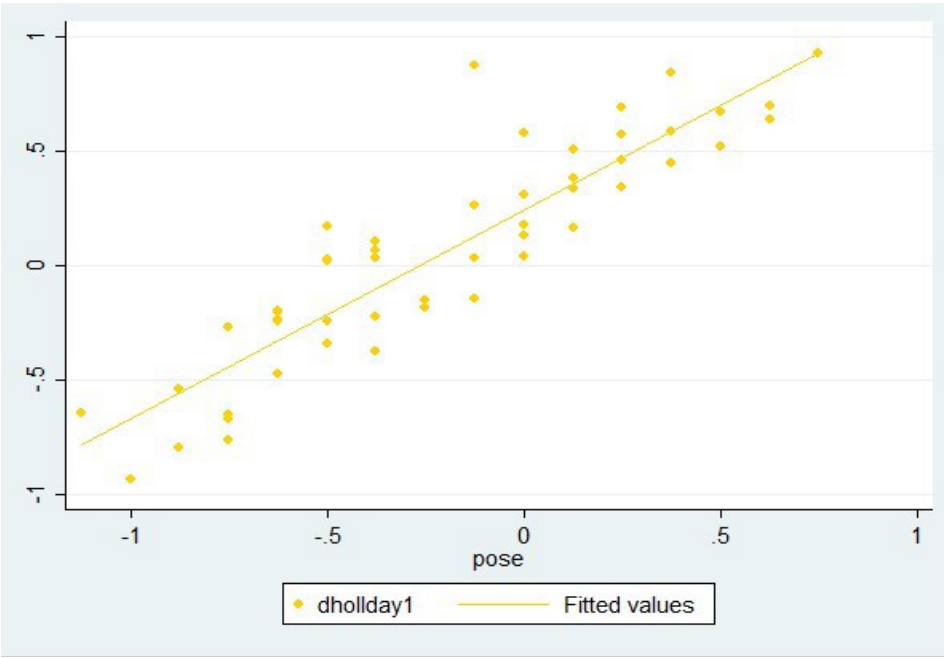

Figure 5.3: Holladay I formula

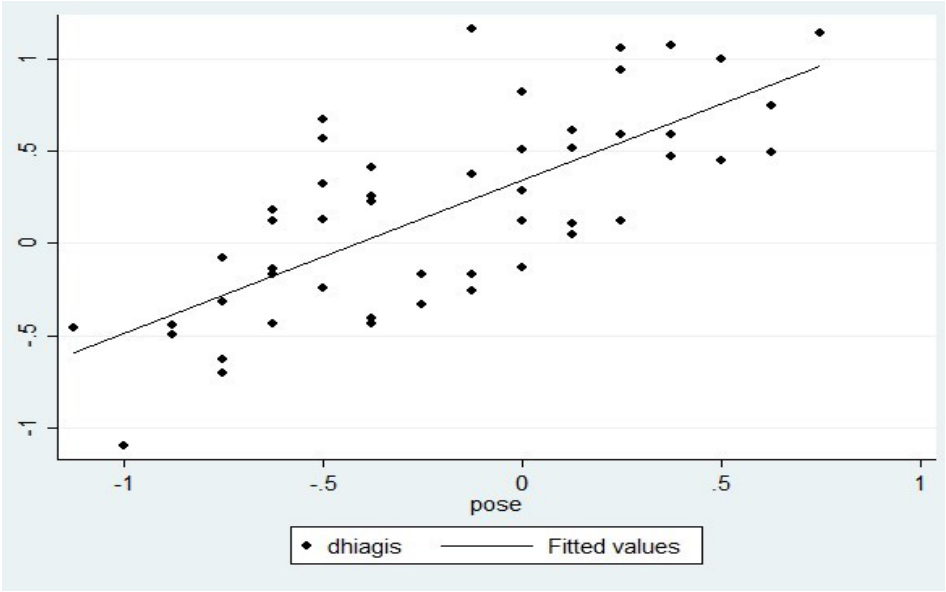

Figure 5.4: Haigis formula

errorsquare	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
method						
2	.0871761	.0649042	1.34	0.181	-.0409196	.2152718
3	.0219826	.0649042	0.34	0.735	-.1061131	.1500783
4	.1069109	.0649042	1.65	0.101	-.0211848	.2350066
pretn	.000997	.0060191	0.17	0.869	-.0108824	.0128765
al	-.0716618	.032474	-2.21	0.029	-.1357528	-.0075708
sex	.0668353	.0625012	1.07	0.286	-.0565178	.1901885
age	.0050405	.0031062	1.62	0.106	-.0010899	.0111709
acd	.0759762	.0880424	0.86	0.389	-.0977854	.2497378
_cons	1.19369	.6372577	1.87	0.063	-.0640094	2.45139

Figure 6: Comparing multiple factors that might affect the refractive outcomes including preoperative IOP, Axial length (AL), sex, age, anterior chamber depth (ACD), AL is the most weighted variable with significant effect to the predicted refractive error (P =0.029). Every 1 mm increase in AL is predicted to result in a 0.07 D decrease in mean error squared (coefficient -0.071).

that could neutralize each other in ME result. So we also have to pay attention at the MES which cannot be neutralized by the negative refractive error.

The most accurate formula is SRK/T, with the least random error (MES=0.216 D) and lowest ME (0.083+-0.45 D). The accuracy of Holladay I is very close to SRK/T in this study (low MES=0.238 D, low ME=0.067+-0.48 D)

Haigis produced the highest MES (0.323 D). This inaccuracy of the Haigis formula may be caused by biometric data using ACD and 3 lens constants that can be changed significantly after cataract removal,[6,7] especially in ACG patients which ACD/AL ratio could be altered from normal anatomy.

However, there is no significant difference between all the 4 formulas. This may be due to the small sample size. (When compare to SRK/T, *P* in Hoffer Q, Holladay I and Haigis are 0.196,0.746 and 0.091 respectively.)

Our result contrasts with a previous study by Jongsoo Joo et al.[8] which concluded that the Hoffer Q formula produced better results than the SRK/T formula in ACG group. This difference could be caused by the small sample size of our study.

AL is the most weighted variable with significant effect to the predicted refractive error (*P* =0.029). Every change of 1mm in AL resulted in reduced MES of 0.07 Diopter and the longer the AL(in this study), the more accurate of the predicted refractive error. This result can be use for subgroup analysis in larger sample size. (Figure 6.)

In a recent article entitled: "Accuracy of intraocular lens calculation formulas" published in the journal Ophthalmology by Ronald Melles et al, Ophthalmology 2018;125:169-178 by the American Academy of Ophthalmology, it shows that the most accurate IOL formula for prediction of refractive outcome at present is the Barrett Universal II formula, even for eyes with short axial length[8]

The main limitation to this study is the instrument used in performing biometry and IOL power calculations is not the most up to date. However, it represents the level of instrumentation that is widely used in routine clinical practice in the region of this study.

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Bleb needling revision with 5-fluorouracil in filtering blebs with chronic failure for over 6 months post-trabeculectomy: a 12-month prospective study

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Purpose: To evaluate the results of bleb needling revision with adjunctive 5-fluorouracil (5-FU) in chronic filtering bleb failure over 6 months post-trabeculectomy.

Method: A prospective study of failed trabeculectomies in a glaucoma clinic between November 2017 and April 2019 were treated with bleb needling revision with 5-FU injection by the same glaucoma specialist and technique. A 27 gauge needle was used to achieve multiple punctures of subconjunctival fibrosis or encystment to attempted elevation of the scleral flap. In all cases, 0.1 ml of 50 mg/ml of 5-FU was then injected subconjunctivally superior to the re-formed bleb, and topical prednisolone acetate and moxifloxacin were prescribed. Success was defined as target IOP achieved and maintained less than 21 mmHg without anti-glaucoma medication at 12 months after first needling. Patients were followed up and re-needled as required.

Results: Needling was attempted on 51 eyes (30 eyes of POAG, 18 eyes of PACG and 3 eyes of secondary glaucoma). The mean number of needling procedures was 1.88 (range 1-10). Needling was successful in 41 (80.4 %) eyes. The average pre-needling IOP was 24.8 ± 12.6 mmHg and the average post needling IOP was 13.5 ± 7.4 mmHg ($P < 0.001$) at 12 months after first needling. The mean number of medications pre-needling was 2.6 ± 1.4 and post-needing was 0.3 ± 0.5 ($P < 0.001$). The mean time post trabeculectomy was 68 months (range 6- 120 months). Prognostic factors for failure of needling revision was pre- needling IOP > 25 mmHg (HR = 3.1, $P = 0.0003$), needling revision ≥ 3 times (HR = 2.6, $P = 0.0012$) and history of repeated filtration surgery before performed this procedure (HR = 1.8, $P = 0.011$). Ten eyes (19.6 %) did not respond to needling; 6 eyes of POAG, 3 eyes of PACG and and 1 eye of secondary glaucoma which required revised trabeculectomy, glaucoma drainage device implantation and anti-glaucoma medication. Three eyes had complications; 2 hyphema and 1 hypotony and no other procedures were required.

Conclusion: Late bleb needling revision with 5-FU injection is still an effective and lasting treatment for the majority of failed trabeculectomy and avoid further surgery included Thai patients. More than one needling is frequently necessary to achieve target IOP. The procedure is relatively safe, with a short operating time and is minimally invasive with less complications.

Conflicts of interest: The author report no conflicts of interest

Key Words: 5-fluorouracil, needling revision, trabeculectomy bleb

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Introduction

The reduction of intraocular pressure (IOP) is aimed at treatment to delay or stop glaucoma progression. Trabeculectomy remains the mainstay of treatment in

medically uncontrolled glaucoma. The use of antifibrotic agents to inhibit wound healing has improved the success rates of trabeculectomy. Despite the advent of antifibrotics, there are significant early and late complications including late failures.[2] Failure of trabeculectomy blebs can occur due to fibrotic proliferation as part of the wound healing response. Surgical failure is reported more frequently in Asian and Afrocaribbean eyes compared to Caucasian eyes, where the fibrotic responses from the former may be exuberant.[3,4] Proper postoperative management is essential for success during the follow up period.[5] Patients with early postoperative failing blebs typically need maneuvers such as digital massage and release of sutures to maintain adequate pressure control. The 5-fluorouracil (5-FU) when given as repeated subconjunctival injection was shown to improved surgical success in patients with high-risk characteristics when given in the early postoperative period.[6] Patients whose bleb fail later usually restart anti-glaucoma medications in an attempt to keep their intraocular pressure (IOP) under control, otherwise a second surgical procedure becomes necessary such as repeat/revise trabeculectomy, the placement of glaucoma drainage device implant or cyclodestructive procedures.[7]

The 5-fluorouracil (5-FU) augmented bleb needling, first described in 1990, is a relatively simple method which can rescue failing blebs.[8] It specifically targets the episcleral and intrascleral fibrosis which occurs in late failing blebs. The procedure can be performed in an office setting at the slit lamp or in the operating theatre. There are varying surgical techniques, most are aimed toward re-opening and maintaining the filtering site and to free scar tissue that is adherent between the conjunctiva and sclera.[9] Bleb needling has been reported to be successfully performed up to 30 years after Trabeculectomy.[10] Some studies have reported results of bleb needling revision in late failed trabeculectomy, however, there is still no data for Thai patients.[3,11] In this prospective study we aim to evaluate the results of bleb needling with adjunctive 5-fluorouracil (5-FU) in chronic filtering bleb failure 6 months post trabeculectomy. Results at 1 year, as well as risk factors of needle revision failure in Thai patients.

Method

The prospective study had the approval of the local Institutional Review Board of waiver of consent and adhered to the tenets of the Declaration of Helsinki. The study was performed in patients with failed trabeculectomy seen in a glaucoma clinic between November 2017 and April 2019 were treated with bleb needling revision augmented with 5-FU injection by one glaucoma specialist and using the same technique.

Chronic filtering bleb failure was defined as inadequately lowered intraocular pressure (IOP) less than 21 mmHg with anti-glaucoma medication or more than 21 mmHg with or without anti-glaucoma medication over 6 months post trabeculectomy as well as presence of a bleb that was encysted, fibrosed, increased vascularity or flattened blebs.

The 5-FU augmented bleb needling was performed at the slit lamp under aseptic technique. The patient's eyelid and periorbital skin were cleaned with 10% providone iodine followed by instillation of tetracaine eye drops and a drop of 5% providone iodine. A lid speculum was inserted. A 27-gauge needle was used to enter subconjunctival space at approximately 8-10 mm distal to the site of failed filtration bleb and incise any Tenon cyst, and on occasion, to slide below the scleral flap and enter the anterior chamber through the filtering ostomy. Once aqueous flow into the bleb is seen, the needle was directed posteriorly and 0.1 ml of 50 mg/ml

of 5-FU was then injected subconjunctivally superior to the re-formed bleb in all cases. Copious irrigation with sterile water and removed the lid speculum. After procedure, the intraocular pressure (IOP) and anterior chamber were checked on the slit lamp. All the patients were instructed to discontinue any anti-glaucoma medication. Topical prednisolone acetate 1% was prescribed every 2 hours while awake for the first week and then 4 times daily. The dose was tapered thereafter according to the clinical appearance of the bleb. Topical moxifloxacin was prescribed for one week in all cases.

Patients were followed up and re-needled as required if the IOP did not reach its goal for each patient based on the severity as well as the history of progression of glaucomatous optic nerve damage or the filtration bleb showed signs of failure such as flattening, encapsulated, cystoid or increase vascularity.

Demographic information obtained included primary trabeculectomy or repeated trabeculectomy with adjunctive MMC in all cases, age, gender, co-morbidities, glaucoma diagnoses, visual acuity, number of needlings and intraocular pressure (IOP) at various time points (month 1, month 3, month 6, month 9 and month 12 post first needling revision with 5 FU injection), any repeat needlings, number of anti-glaucoma medications and any further surgical intervention were recorded. Exclusive criteria consisted of age < 20 years old, patients who were pregnant or breast-feeding, patients who were unable to give informed consent and those who had subconjunctival injection of 5-FU without bleb needling.

The intraocular pressure (IOP) was measured using the same Goldmann applanation tonometry and slit lamp for every patient on every visit. Success was defined as maintenance of IOP $\geq$ 6 mm Hg and $\leq$ 21 mmHg in absence of further surgery or without anti-glaucoma medication at 12 months after first bleb needling revision with 5-FU injection. The use of any anti-glaucoma medications, repeat trabeculectomy or glaucoma drainage device, adjunctive laser treatment with Selective Laser Trabeculoplasty (SLT) would constitute as a needle revision failure at 12 months after first needling revision. Hypotony was defined as an IOP of less than 6 mmHg.

Statistical analyses were performed using IBM SPSS statistic version 19.0 (IBMcorp, Armonk, NY, USA). Mean with standard deviation (SD) were calculated for continuous variables and frequency with percentage were tabulated for categorical variables. Student's t-test was used for continuous variables and chi-square test or Fisher's exact test for categorical variables. Cox regression analysis was performed to calculate the hazard ratios of possible factors that may lead to bleb failure using Stata version 11.1. All reported values were compared at a significance level of 0.05.

Result

Fifty-two eyes of 52 patients were enrolled in the study. One eye was excluded as they relocated. Population consisted of 23 males (45%) and 28 females (55%) in Thai patients. Needling revision with 5-FU injection was attempted on 51 eyes of 51 consecutive patients. Glaucoma diagnosed included primary open angle glaucoma (POAG) in 30 eyes (59%) primary angle closure glaucoma (PACG) in 18 eyes (35%) and secondary glaucoma of 3 eyes (6% included 2 traumatic glaucoma, 1 uveitic glaucoma).

Twenty-seven (53%) of 51 eyes were phakic and 24 eyes (47%) were pseudophakic. Primary trabeculectomy had been performed in 33 eyes (64.7%) and 18 eyes (35.3 %) had undergone repeat trabeculectomy. The mean age of the 51 patients was 62.7 ± 21.4 years (Range

32-80). The demographics of the study population were listed in Table 1.

The mean number of needle revision was 1.88 (Range 1-10). The mean time since the trabeculectomy to first needling revision was 68 ± 32 months (Range 6- 120 months). The time interval between the trabeculectomy and first needling revision had no predictive effect on outcome of the needling between the success group and failure group. (Table2)

Needling had been successful in 41 (80.4 %) eyes and had failed in 10 eyes (19.6 %). The mean pre-needling IOP was 24.8 ± 12.6 mmHg and 13.5 ± 7.4 mmHg at 12 months post first needling. The IOP was significantly reduced from first month throughout 12 months post first needle revision with 5-FU injection ($P < 0.001$). The IOP was steady and maintained at 12 months (Figure1). The average number of topical medications taken before needle revision was 2.60 ± 1.4. At 6 months and 12 months, the average number of topical glaucoma medications used was 0.3 ± 0.5 both time period. There was a statistically significant decrease in number of glaucoma drugs at 1 month to 12 months ($P < 0.001$, Figure 2). However, there was no difference between the number of medications used at baseline between the success group and failure group ($P > 0.05$, Table 2).

Characteristics of patients with success and failure following needling revision with 5-FU injection were prescribed in Table 2. The two groups were similar in age, gender, type of glaucoma, mean number of pre-needling glaucoma medication, lens status and pre-needling bleb morphology. However, significant differences were found in three variables between the two groups when a multivariate analysis using Cox proportional hazard regression analysis was performed. Prognostic factors for failure of needling revision with 5-FU injection were listed in Table 3 included pre- needling IOP > 25 mmHg (HR =3.1, P= 0.0003), ≥ 3 previous needling revisions (HR = 2.6, P = 0.0012) and history of repeated filtration surgery before performed this procedure (HR = 1.8, P = 0.011).

The morphology of failed blebs that required revision needling consisted of 13 encapsulated (25.5%), 12 flattened (23.5 %), 12 cystoid (23.5) and 14 increased vascularity (27.5 %). Bleb morphology was not a prognostic factor for failure of needling revision. Thirty-one eyes had previous ocular surgery other than trabeculectomy including phacoemulsification in 24 eyes and pterygium excision with conjunctival auto-graft in 7 eyes.

Ten eyes (19.6 %) that did not respond to at least 3 episodes of needling and required additional glaucoma treatment consisted of 6 eyes of POAG, 3 eyes of PACG and 1 eye of secondary glaucoma. Four eyes required revised trabeculectomy, 2 eyes required glaucoma drainage device implantation and 4 eyes required anti-glaucoma medication. Complications following revision needling with 5-FU injection was found in 6 (11.8%) of 51 eyes. Minimal gross hyphema was observed in 2 eyes and non-sustained hypotony was found in 1 eye. There were no other procedures required in these three eyes. Three eyes of 27 phakic eyes (11%) had lost greater than 2 lines of visual acuity in the Snellen chart compared with the pre-needling group at 6 months due to dense posterior subcapsular cataract. All three of these eyes subsequently underwent cataract surgery with good recovery of vision 20/40 to 20/30 at 12 month and success IOP control without any anti-glaucoma medications. There were no serious sight threatening complications or ocular surface problems found such as bleb leakage, flat anterior chamber, choroidal effusion, suprachoroidal hemorrhage, aqueous misdirection, endothelial decompensation, endophthalmitis, and filamental/punctate keratitis.

Table 1: Patient demographics

Demographics	Number	Percent
Age (years old)	62.7 ± 12.4 (Range 32-80)	-
Gender (person)		
- Male	23	45
- Female	28	55
Type of glaucoma (eye)		
- POAG	30	59
- PACG	18	35
- Secondary glaucoma	3	6
Underlying disease (person)		
- None	24	67
- Diabetic mellitus	3	8
- Hypertension	5	14
- Dyslipidemia	4	11
Lens status		
- Phakic	27	53
- Pseudophakic	24	47
Pre-needle revision bleb morphology		
- Encapsulated Flattened	13	25.5
- Cystoid	12	23.5
- Increase vascularity	14	27.5
Filtration surgery		
- Primary trabeculectomy	33	64.7
- Repeat trabeculectomy	18	35.3

Table 2: Characteristics of patients with success and failure following needling revision with 5-FU injection

Characteristics	Success (n= 41 eyes, 80.4%)	Failure (n = 10 eyes, 19.6 %)	*P*
Age (mean ± SD)	62.5 ± 10.4	62.9 ± 5.8	0.924
Gender Male Female	 18 23	 5 5	 0.462
Time interval to first needling (months)	67 ± 36 (Range 6-114)	69 ± 42 (Range 36 -120)	0.944
Mean number of needling revision	1.8	3.2	0.0012
Type of glaucoma (eye) POAG PACG Secondary glaucoma	 24 (58.5 %) 15 (36.6 %) 2 (4.9 %)	 6 (70.0 %) 3 (30.0 %) 1 (10.0 %)	 0.554
Mean pre-needling IOP (mmHg)	22.4	32.2	0.0003
Mean pre-needling glaucoma medication	2.3 ± 1.7	2.6 ± 1.4	0.956
Lens status Phakic Pseudophakic	 22 (53.7%) 19 (46.3%)	 5 (50%) 5 (50%)	 0.536
Pre-needling bleb morphology Encapsulated Flattened Cystoid Increase vascularity	 11 (26.8 %) 9 (22.0 %) 10 (24.4%) 11 (26.8 %)	 2 (20.0 %) 3 (30.0 %) 2 (20.0 %) 3 (30.0 %)	 0.403
Filtration surgery Primary trabeculectomy Repeat trabeculectomy	 31 (75.6 %) 10 (24.4 %)	 2 (20.0 %) 8 (80.0 %)	 0.011

Chi-square and Fisher's exact test for categorical groups and independent t test for continuous variables

Table 3: Risk factors for failure of needling revision with 5-FU injection: Coefficients and risk estimated per Cox Proportion Hazard Regression Model

Prognostic factor	Coefficient ± Standard error	*P*	Hazard Ratio	95% CI on Risk Ratio	
				Lower	Upper
Pre- needling IOP > 25 mmHg	1.25 ± 0.33	0.0003	3.1	1.5	6.6
Needling revision ≥ 3 times	1.05 ± 0.31	0.0012	2.6	1.3	5.4
Repeated filtration surgery	0.79 ± 0.29	0.011	1.8	1.1	4.1

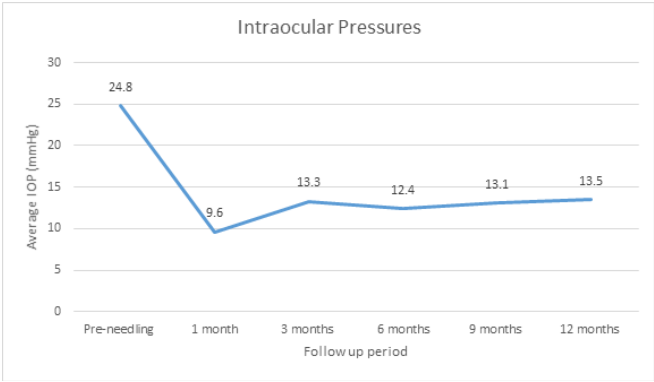

Figure 1: Mean intraocular pressure (mmHg) pre- and post-needling with 5-FU injection at all time intervals after first procedure

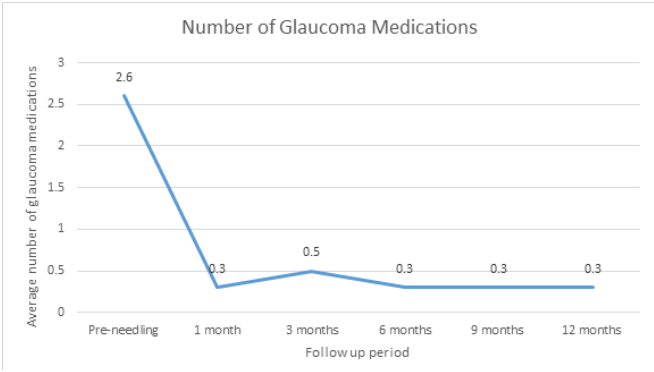

Figure 2: Mean number of topical glaucoma medications pre- and post-needling with 5-FU injection at all time intervals after first procedure

Discussion

The most common cause of trabeculectomy failure is scarring. Treatment of elevated intraocular pressure after surgery include digital massage, release of sutures early, reuse of topical anti-glaucoma medication, laser procedure (SLT, ALT), needle revision or repeated trabeculectomy if the bleb continues to fail after a period of time.[7]

The use of 5-FU in needling revisions exhibited an effective outcome in many studies if performed early in the postoperative period.[7,8,12] Repeating injections and needling are often necessary to achieve successful outcomes.[13] Variable success rates have been reported in the literature. It is difficult to make comparisons across the studies due to different study lengths, sample size, definition of success and antimetabolite used. Ewing and Stamper first reported 91.7% overall success in a small sample of 12 cases using 5-FU augmented bleb needling in 1990.[8] Success in their study was defined as target IOP achieved with or without use of topical medications. The mean follow up was 9 months. In some studies, the success rates range from 54% to 84% at 1 year, depending on different definition of success and case selection.[13,14,15,16,17]

In the present study, we reported efficacy of this procedure in chronic filtering bleb failure over 6 months after trabeculectomy in Thai eyes with 80.4 % success rate without serious visual threatening complications. We also reported on factors associated with procedural failure. This report is the first and largest prospective cohort study of 5-FU augmented bleb needling performed in Thai patients.

Makornwattana *et al* reported a success rate of 100 % of multiple needle revisions and 5-FU injection in over 14- month old dysfunctional blebs to achieve IOP less than 21 mmHg without anti-glaucoma medication for at least 3 months post-interventional in case series of 8 Thai patients.[11] Our prospective study included 51 eyes all of which had undergone a needle revision with 5-FU injection. Success was defined as the same criteria to the aforementioned study with the difference that our study has a 12 month follow up period after initial needling. Our success rate was 80.4%, which supported the efficacy and safety of needle revision augmented with 5-FU injection in chronic dysfunctional blebs in Thai patients. Moreover, we also identified the 3 risk factors for the failure of a needling procedure included pre- needling IOP > 25 mmHg, needling revision ≥ 3 times and history of repeated filtration surgery before performed this procedure.

Prutthipongsit *et al* reported an overall success rate of 82.69 % in both acute and late failure of filtration blebs at 6 months follow up in a retrospective study in Thai patients.[12] However, this study defined outcomes as complete success (target IOP < 21 mmHg without topical glaucoma medication and no addition of other surgical procedures), qualified success (IOP < 21 mmHg with topical glaucoma medications) and failure (IOP> 21 mmHg together with the execution of other surgical procedure). Pre-needling IOP > 25 mmHg and secondary glaucoma were the risks factors of failure of 5-FU needling in this study, supported our prospective study results in a 12 month follow up period.

Our finding showed 80.4% of patients benefited from the late bleb needling revision as a surgical adjunct. The length of the interval between the surgery and needling revision had no predictive effect on outcome of the needling. The role of previous repeated filtration surgery is interesting. The patients who experience a repeated filtration surgery had a risk factor of failure of needle revision. This suggests bleb revision by needling is an effective procedure to prevent subconjunctival fibrosis from filtration surgery with potentially improved success rate of

repeated filtration surgery in the future. On the other hand, when performing bleb needling revision, one should be aware of failure in repeated trabeculectomy.

Shin *et al* identified risk factors for failure of 5-FU needling revision for failed conjunctival filtration blebs included pre-needling IOP > 30 mmHg, lack of MMC use during the previous filtration surgery and IOP > 10 mmHg immediately following needling revision.[19] This study reported a cumulative success rate of 45% at 1 year, 33% at 2 years and 28% at 4 years. Our study exhibited more success rate at 1 year than this study maybe due to the use of adjunctive MMC in all cases, both primary trabeculectomy and repeated trabeculectomy in our study. The lower rate of success than our study is propositionally due to the study population being African American ethnicity, who have been shown to have a greater tendency for poor pressure control following surgery.[14] Other issues may be due to a different definition of success in each study, the longer duration follow up time in our study, in which failure of the trabeculectomy bleb can occur due to fibrotic proliferation as a part of the wound healing response.[3,4] However, a higher pre-needling IOP is associated with failure, which is in agreement with our study and Tsai AS et al. [21] that supported the use of MMC during the original glaucoma filtration surgery seems to be a beneficial factor in the future success of 5-FU needling revision due to long lasting on local fibroblasts. [19,20]

Tsai AS *et al* reported complete a success rate of 62% in POAG and PACG at 12 months. In addition to a success rate of 57.9% for POAG and 63.0% in PACG at 24 months with the same criteria of success as our study which defined as IOP ≤ 21 mmHg in absence of further surgery or use of anti-glaucoma medications.[21] This study recruited 175 eyes with mean needling attempts 1.9 ± 1.4 and 2 ± 1.6 for POAG and PACG respectively. Most of the population were Chinese ethnicity (72% in POAG, 81.4% in PACG). The mean interval between filtration surgery and bleb needling was 299.9 ± 616.4 days for POAG and 167.1 ± 272.2 days in PACG. The success rate between POAG and PACG were not significantly different and a higher pre-needling IOP were associated with failure, which supported the results in Thai patients in our study. Asian eyes have a greater propensity for scarring.[3,4] However, the results in Singapore and Thailand revealed that bleb needling revision with 5-FU injection which performed in chronic bleb failure can rescue and restore bleb function in Asian eyes.

Several risk factors for failure of 5-FU needle revision were identified, including lack of mitomycin C (MMC) use during the initial filtration surgery,[19] fornix based trabeculectomies,[22] pre-needling IOP >30 mmHg,[7,18] IOP >10 mmHg immediately following needling revision,[7,14,19] and elevated bleb with highly vascularized or microcysts.[16] In our study, we found that needling revision more than 3 times was a great risk factor associated with needling revision failure. This is similar to previous studies by Tsai AS *et al*[21] and Wong *et al*[23] which also studied in Asian eyes. Bleb needling can in itself induce inflammation and fibrotic proliferation, an increase in the number of needling procedures suggest that eyes undergoing this procedure have a greater propensity to scar.

Lee *et al* reported a flat central bleb and flat bleb height were risks factor of needle revision failure in Taiwanese eyes with 23 months follow up period.[24] Rotchford and King also identified a flat bleb was a risk factor of failure with 41 months follow up period in United Kingdom.[16] In our present study, there was no significant difference of pre-needling bleb morphology between the success and failure group.

Bleb needling is a relatively safe

procedure.[7,21] Complications are mostly minor and consist of conjunctival wound leak, small hyphema, corneal epithelial toxicity and transient shallow of anterior chamber. Visual threatening complications include significant hypotony, suprachoroidal hemorrhage, malignant glaucoma, endophthalmitis related to blebitis can occur but are rare. Zeng L *et al* performed needling revision in operating theater in all cases to easy to resolve complication during procedure such as bleb leak, flatten anterior chamber.[17] Mercieca K *et al* performed a cross-sectional online survey distributed to glaucoma specialists in United Kingdom, they reported bleb needling was performed in the operating room by 56 % of responders.[25] In our study, although we performed this procedure at the slit lamp in all cases, there were no major visual threatening complications found. Needling revision is a safe and simple method which can rescue failing blebs.[8] In our study, there were no serious corneal toxicity from 5-FU injections which may be prevented by a copious irrigation with sterile water in all cases and only an average 1.8 injection of 5-FU. Copious irrigation with a sterile water is recommended in all cases.[11]

Three of 27 phakic eyes (11%) lost visual acuity greater than 2 lines on Snellen chart compared with the pre-needling level at 6 months due to dense posterior subcapsular cataract. Zenq *et al* reported 24% had cataract surgery after needle revision surgery.[17] The development of cataract post-trabeculectomy and needle revision is another significant issue. All three patients in this study subsequently underwent cataract surgery with good recovery of vision 20/40 to 20/30 and success IOP control without any anti-glaucoma medications at 12 months. However, after cataract surgery, the risk of bleb failure increases 8-fold with expected survival time reduced from 190 weeks to 34 weeks in previous study.

Although we performed a prospective study, our study has some limitations pertaining to the non-randomized methodology and the lack of a control group. Moreover, the repeated needling revisions depended on the clinician's judgement during 12 months follow up period. In addition, no objective bleb grading system has been used to describe the morphologic features. Three eyes with secondary glaucoma may interfere the results of primary glaucoma and the goal of success is the IOP of less than 21 mmHg may not be safe for advanced glaucoma patients. Future randomized control trials are required to reduce bias. Extension of follow up over 12 months post initial needling and clarification of objective bleb grading system and inclusion of only primary glaucoma patients and defined the definition of success depending on the severity of glaucoma are recommended in future studies.

Conclusion

Late bleb needling revision with 5-FU injection is still an effective and lasting treatment for the majority of failed trabeculectomies and avoid further surgery in Thai patients. Risk factors for failure of the initial 5-FU needling revision included pre- needling IOP > 25 mmHg, needling revision ≥ 3 times and history of repeated filtration surgery before performed this procedure. More than one needling is frequently necessary to achieve treatment goals. The procedure is relatively safe, with a short operating time and is minimally invasive with infrequent complications.

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Efficiency in skill development of pterygium excision with amniotic membrane transplantation among the 1st year ophthalmology residents at Thammasat Eye Center

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Purpose: To evaluate the learning curve of pterygium excision with amniotic membrane transplantation among the 1st year ophthalmology residents.

Methods: Prospective comparative study. Four first year ophthalmology residents were monitored for operating time and recurrence rate on all their cases of pterygium excision with amniotic membrane transplantation throughout one year. Data for baseline characteristic of patients with continuous data were analyzed for differences among residents using one-way ANOVA. Proportional data such as age, gender, laterality and recurrence rate were analyzed for differences among residents using Fisher's exact test. Average predicted operating time with consecutive cases were analyzed using linear regression. Operating time stabilization with consecutive cases was visualized by a Locally Weighted Scatterplot Smoothing (LOWESS) and Quadratic best fit lines.

Results: A total of 159 eyes (159 patients) with primary pterygium excision were performed with sutured amniotic membrane transplantation. All cases were attributed to four ophthalmology residents composed of 40, 41, 42 and 36 patients. The average operating time was 50.38 ± 13.92 minutes, with a range of 28 to 100 minutes. The operating time declined in proportion to the number of patients and stabilized after 38 cases (average time 43.33 ± 18.93 minutes). The recurrence rate of pterygium found in this study was 11.94%

Conclusions: Pterygium excision with sutured amniotic membrane transplantation is considered as appropriate training procedure for ophthalmology residency training due to less duration needed to reach the learning curve. Additionally, the rate of recurrence among residents is comparable to that of other similar studies.

Keywords: learning curve, operating time, pterygium excision, amniotic membrane transplantation, recurrent pterygium

Ethics: This study was approved for ethical research in human with the human research ethics committee of Thammasat University, Thailand (Research ID: MTU-EC-OP-0-105/56)

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Introduction

Pterygium is a degenerative disease of the ocular surface tissue. Many mechanisms have been proposed such as proinflammatory cytokines[1], immunological mechanism,

many of which are significantly driven by ultraviolet light and some suggested involvement of genetic factors. [2,3,4] Its prevalence is high in the tropical area near the equator with significantly more sunlight exposure.[5-8] Local climate and weather with windy, dusty, and smoky environments are also associated with higher prevalence for pterygium occurrence.[5] Some reported the influence of age resulting in younger patients being more likely to experience a recurrence.[8] Other factors such as gender are not found to be statistically proven.[9] One important part in managing patients with pterygium is the avoidance of predisposing factors such as ultraviolet from sunlight and wind exposure. In the past, bare sclera technique with or without adjunctive treatment such as β- radiation or MMC (Mitomycin C) was frequently performed in routine service. [10] However, later studies found the recurrence rate to be up to 50%.[11-13] In current practice, after pterygium excision, the bare sclera is covered by either a conjunctival graft (CAG)[10-11,14-17] or amniotic membrane transplantation (AMT)[16-18] resulting in a lower recurrence rate of approximately 5-10%. Conjunctival graft has more appealing cosmetic result in exchange for the loss of normal conjunctival tissue which might be needed for future glaucoma surgery.[11] Amniotic membrane does not require the use of the patient's normal conjunctiva. Some studies still report a higher recurrence rate by amniotic membrane compared to conjunctival graft.[9] Pterygium excision with amniotic membrane transplantation is limited by the varied availability of amniotic membrane. Surgeons place the amniotic membrane onto the sclera using either sutures or fibrin glue. Both techniques are still widely used. No reports are found to give differences to outcome.[21] Comparing both techniques that fibrin glue requires less time and a relatively flatter learning curve than the sutured technique.[19-21] Pterygium is the second most common eye disease requiring surgical treatment (second only to cataracts).[22] Pterygium excision operation is popularly used for resident training due to its complexity and less debilitating complications compared to cataract surgery in most ophthalmology residency training centers.[23] Therefore pterygium excision is an essential part of ophthalmology residency programs. It is necessary to study various factors associated between the learning curve and proficiency development of surgical procedures by residents for improving ophthalmology residency programs.

Materials and methods

One hundred and fifty-nine patients with pterygium (total of 159 eyes) were enrolled in the study. All pterygium cases in this study were screened by ophthalmologists for indication of surgery. Four first year residents were chosen to participate in this study. All procedures were conducted during October 2014 to July 2015 at Thammasat eye center. Prior to surgery patients were interviewed and underwent complete ocular examinations. All pterygium excisions were performed with sutured amniotic membrane graft in this study.

Patient selection

Inclusion criteria

1.Eye diagnosed with primary pterygium by a consultant level ophthalmologist.
2.Patients aged between 20 to 70 years old.
3.Pterygium with cornea invasion ≥ 2 mm.
4.Patients informed and consented to surgery.
5.Patients able to attend follow-up at least 6 months postoperatively.

Exclusion criteria

1.Patients with multiple pterygium heads in one eye.
2.Eyes with history of prior ocular surgery, active ocular inflammation,

infection, preexisting glaucoma or any other severe ocular disease. 3.Patients with underlying disease contraindicating for surgery such as recent onset heart attack, cerebrovascular disease. 4.Patients unable to cooperate during surgery. 5.Patients unable to consent for follow according to study protocol.

Pre-operative care

The patient history was fully taken especially on the patient occupation, UV exposure behavior (indoor and outdoor), duration and onset of pterygium, prior ocular surgery or ocular accident. Full ocular examination was performed such as visual acuity assessment, intraocular pressure measurement, complete fundus examination and slit lamp biomicroscopy to evaluate the appearance and size of pterygium on the cornea in millimeters.

Surgical technique

First the eyelid was painted with 5% povidone-iodine solution which was also used for eye irrigation. The patient's eye was draped and prepared by sterile technique. Draping was done to reduce the non-surgical exposure area. Anesthetic technique consisted of topical 0.5% tetracaine hydrochloride eye drop together with subconjunctival 2% xylocaine without adrenaline injection under the pterygium body. The pterygium head was excised from the cornea. Bleeding point was checked and stopped with cotton bud tip or by bipolar coagulator. Bare sclera was measured to tailor the size of the amniotic membrane graft. The graft was placed on bare sclera also with epithelium facing upward only. Single suture by 8-0 or 10-0 nylon was firstly done at the four corners of the amniotic membrane graft fixing to the sclera followed by continuous sutures all along graft margins. Operating time was recorded in minutes, starting from subconjunctival xylocaine injection to the last nylon suture. Cases which any intraoperative complications have occurred were thoroughly recorded.

Post-operative care and follow-up

Patients were routinely follow-up appointments on the first day, week 1, month 1, month 3 and month 6 after pterygium surgery respectively. All received topical steroid and antibiotic eye drops and eye ointments. Drug administration and dose adjustment depended on the inflammation of the eye postoperatively. Patients were advised to avoid from wind, dust and sunlight by wearing sunglasses all the time. Visual acuity assessment, intraocular pressure measurement was done together with slit lamp biomicroscopy was performed to detect inflammation and infection of the amniotic membrane in addition to recurrence of pterygium at each follow-up visit.

Statistical analysis

Prospective comparative study. Four first year ophthalmology residents were monitored for operating time and recurrence rate throughout one academic year. Data for baseline characteristic of patients with continuous data was analyzed for differences among residents using one-way ANOVA. Proportional data such as gender and recurrence rate were analyzed for differences among residents using Chi-squared test. Average predicted operating time with consecutive cases was analyzed by linear regression. Operating time stabilization with consecutive cases was visualized by a Locally Weighted Scatterplot Smoothing (LOWESS) and Quadratic best fit lines.

Results

All four residents were divided into groups A, B, C, and D as shown in table 1. All performed pterygium excision with sutured amniotic membrane transplantation in patients who were qualified by the inclusion criteria. Patients who did not

meet the criteria were excluded from the study. The surgery took place between October 2014 and July 2015. The number of patients in each group was 40, 41, 42 and 36 respectively. The average age of patient was 57.32 ± 13.15 years old. Of the 159 patients, 68 patients (42.76%) were male and 91 patients (57.23%) were female. The site of pterygium occurred was 83 (52.21%) on the right and 76 (47.79%) on the left respectively. Overall the information on number of patients, gender and laterality distribution did not show statistical differences. The shortest duration from onset of pterygium to surgery day was 6 months and the longest duration was 11 years. 10-0 nylon were mostly used for suturing in 147 patients (92.50%) while the rest 12 patients (7.55%) were sutured by 8-0 nylon. Recurrent pterygium within 6 months was found in 19 patients (11.94%). The average operating time was 50.38 ± 13.92 minutes with a range of 28 minutes to 100 minutes.

In figure 1 The LOWESS (Locally Weighted Scatterplot Smoothing) best fit line showed decreasing operating time for pterygium surgery in correspondence to the increasing number of cases. The incline of the best fit line gradually stabilized. The operating time appeared to stabilize on 40 minutes at about 38 cases visually extrapolating from this graph.

In an alternate attempt to model the learning curve from Figure 2 (Quadratic prediction model), the standard deviation of operating time represented on the vertical bars. The average operating time of all resident's first case was 75.00 ± 10.80 minutes. The operating time became gradually shorter by each consecutive case. Visually extrapolating from the Quadratic prediction model the operating time appeared to stabilize on 43 minutes at about 38 cases.

Comparing both attempts to model the learning curve at which the operating time stabilized, we found that both models are relatively consistent. Visual extrapolation of the LOWESS and Quadratic model both suggested operating time stabilization at the 38th case with operating time of about 40 and 43 minutes respectively. This was also consistent with raw data analysis and the average of the 38th case for all 4 surgeons was 43.33 ± 18.93 minutes.

In an attempt to model the progression of operating time among residents using generalized linear regression model in figure 3A,3B,3C,3D, we found that each resident spent less time

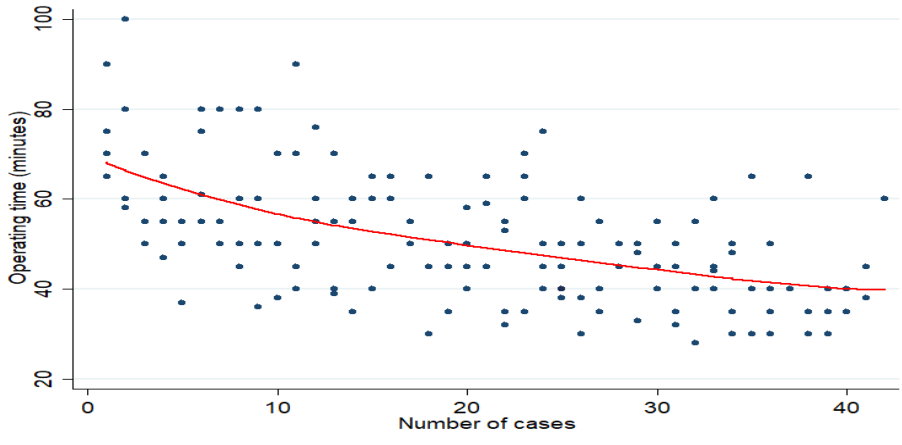

Figure 1: Operating time of pterygium excision with increasing number of cases, with LOWESS (Locally Weighted Scatterplot Smoothing) best fit line.

Table 1: Descriptive statistics in demographic data between the groups.

	A	B	C	D	Total	*P*
Number	40	41	42	36	159	0.885
Age (years old)	52.30±12.86	55.75±13.56	59.09±13.37	62.77±10.46	57.32±13.15	0.004
Affected eye						
OD	21 (52.50%)	19 (46.34%)	23 (54.76%)	20 (55.55%)	83 (52.21%)	0.763
OS	19 (47.50%)	22 (53.66%)	19 (45.24%)	16 (44.45%)	76 (47.79%)	
Gender						
Male	19 (47.50%)	17 (41.46%)	17 (40.47%)	15 (41.67%)	68 (42.76%)	0.922
Female	21 (52.50%)	24 (58.54%)	25 (59.53%)	21 (58.33%)	91 (57.23%)	
Operating time (minutes)	49.07±14.68	51.96±12.81	54.90±13.29	44.80±13.32	50.38±13.92	0.010
Suture						
10-0	40 (100.0%)	41 (100.0%)	38 (90.47%)	28 (77.78%)	147 (92.45%)	0.000
8-0	0 (0.00%)	0 (0.00%)	4 (9.53%)	8 (22.22%)	12 (7.54%)	
Number of recurrent pterygium	8 (20.00%)	4 (9.75%)	3 (7.10%)	4 (11.11%)	19 (11.94%)	0.348

according to the number of surgeries.

Graph in figure 5 was a linear regression model stratifying the number of cases into strata of 3 cases for visualization. By comparing the reduced operating time taken by each resident in the same graph shown in figure 4 and 5 (linear regression and standard error bars), all residents could be divided into 2 groups based on their similarity upon comparison of operating time (B, D and A, C). Group B and D appeared similar in operating time within the first 6 cases by faster than that of group A and C. Operating time was similarly comparable reduced in all 4 residents after the 6th case of onwards.

Of 159 eyes, 19 eyes were found to have recurrence (11.94%). The recurrence rate of each resident A, B, C, and D was 20.00 %, 9.75 %, 7.14 % and 11.11% respectively shown in table 2. Other complications noted in this study are shown in table 3 such as Dellen 1 patient (0.63%), Tenon prolapse 1 patient (0.63%), Corneal scar 6 patients (3.77%), Graft retraction 1 patient (0.63%), Epithelial cyst 1 patient (0.63%), and Pterygium granuloma 1 patient (0.63%).

Discussion

This study on surgical skill development of ophthalmology residents focused in pterygium excision with amniotic membrane transplantation is evaluated by operating time. Several studies were conducted on this topic. A study from Ramsay et al. (2001), Cook et al. (2004) had concluded various statistical methods used for learning effects in health technology.[24-25] The common term used was the relationship between the decreasing rate of operating time together with the occurrence rate of the complication. With regards to this study, the complication of interest is the recurrence rate of the pterygium after surgery. However due to the natural pathophysiology of this disease, there are

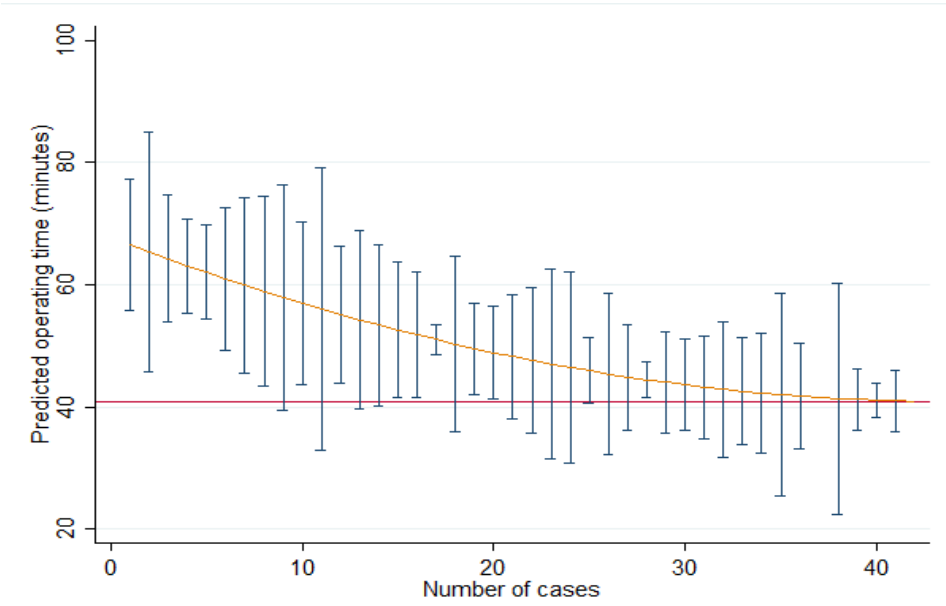

Figure 2: Predicted operating time with increasing number of cases, with Quadratic prediction model. Vertical bars represent standard deviation of operating time.

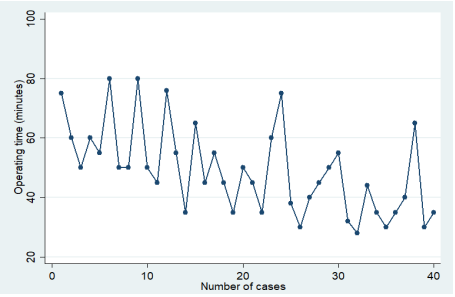

Figure 3A: Pterygium excision operating time with increasing number of cases, Surgeon A.

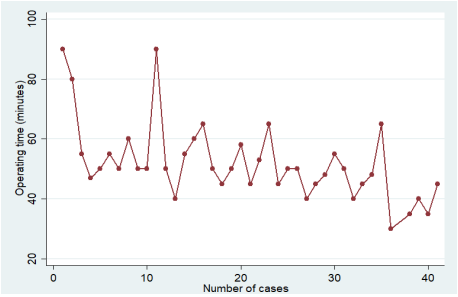

Figure 3B: Pterygium excision operating time with increasing number of cases, Surgeon B.

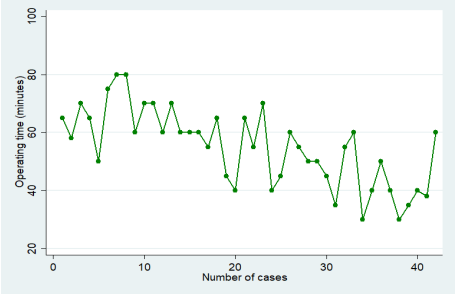

Figure 3C: Pterygium excision operating time with increasing number of cases, Surgeon C.

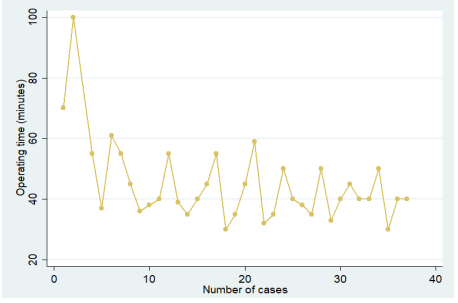

Figure 3D: Pterygium excision operating time with increasing number of cases, Surgeon D.

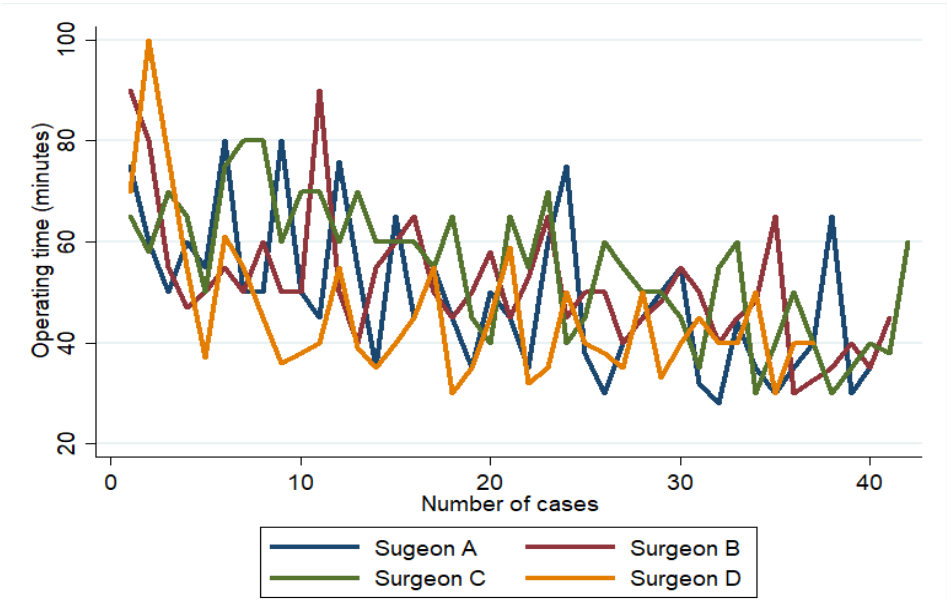

Figure 4: Pterygium excision operating time with increasing number of cases, separated by 4 surgeons.

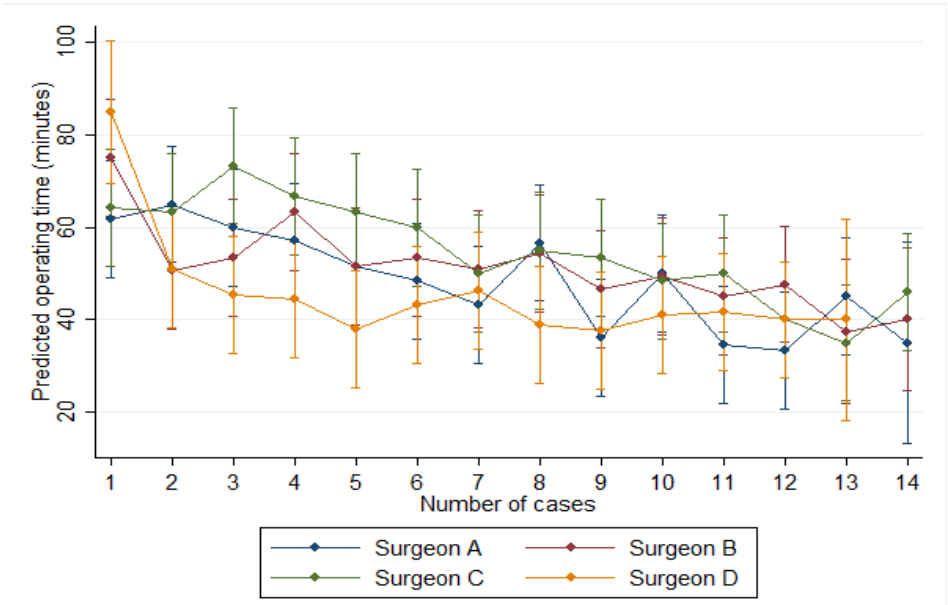

Figure 5: Predicted operating time with increasing number of cases, (in strata of 3) with linear regression and standard error bars.

multifactorial etiologies involving the recurrence rate.[26] The recurrence rate may not be the best surrogate marker for skill development in pterygium surgery during residency program training. The surgeon's expertise is one of many factors determining the learning curve. If we ignore confounding factors as complication rates and variations in intrinsic difficulties of each case ranging from anatomical to cooperative factors, the learning curve of pterygium surgery can only be followed by the decreased in operating time alone.[24]

Statistical methods to model the learning curve in studies widely used for the decreased operating time analysis was Wright and Logarithmic curve fitting of operating time data.[24] The rate of decrease in operating time during the initial phase could determine the learning curve. Wright's learning percentage was popularly used to analyze the efficacy of work in manufacturing industry which used a value as high as 80-90%.[24] However the average operating time also reflect the personal character of surgeon more than the difficulty of the surgical method.

Koranyi G. et al. observed 120 cases of pterygium surgery with the cut and paste method and quantified outcomes of learning curve development by measuring operating time and recurrence rate.[27] The study found that in surgeons with no prior experience in pterygium surgery under the microscope had the learning curve for achieving stability around 40 cases. The steepness of the learning curve for the cut and paste method was not clinically different from the surgeons experienced in cataract surgery under the microscope previously.

The objective in our project is to study the relationship between the decreasing rate of operating time and the number of surgical cases need to reach the learning curve that representing skill development in inexperienced ophthalmology resident. In figure 1 we plotted the graph by using the LOWESS (Locally Weighted Scatterplot Smoothing) best fit line to visualize the average operating time by the four ophthalmology residents. The average operating time in the first case of each resident was approximately 75.00 ± 10.80 minutes. This operating time decreased until the 38th consecutive cases and thereafter the average operating time had stabilized.

We then later plotted another graph (figure 2) using Quadratic prediction model to alternately visualize the operating time in relation to the number of consecutive cases. Visual extrapolation of both models showed that the average operating time by the ophthalmology resident was around 40 and 43 minutes respectively at the 38th case and was maintained stable even after consecutive cases. This leads to the understanding of the resident's learning curve used for pterygium excision with amniotic membrane transplantation was after 38 cases onwards. This result was similarly to the study from Koranyi G. et al. which reported the learning curve needed at 40 cases.[27] In our study the pterygium cases per each resident that can operate upon is around 36 to 42 cases which is insufficient to clearly assess the resident's skill development. But we can monitor and predict operating time from the graph trend statistically. For further studies this limitation may continue to be resolved by collecting more samples.

Figure 4 and 5 showed operating time comparison between the four residents. We found that surgeon B, D had a faster learning curve than surgeon A, C (although this was only observation in the first 6 cases). Suggesting that learning curve is a combination of various factors surrounding the experience of surgery, there are also factors that fluctuate between the surgeons themselves. The variable between the surgeons appear impactful only at the beginning of the training. When the ophthalmology resident has experienced a

Table 2: Show the recurrence of pterygium, describing the incidence and the chronological case number of which it occurred, and the proportion of recurrences that occurred in the first 10 cases for each surgeon.

Resident	Number of pterygium recurrence	Chronological case number of pterygium recurrence	Number of pterygium recurrence in the first 10 cases
A	8 (20.00%)	2,3,6,8,10,15,21,25	5 (62.5%)
B	4 (9.75%)	3,4,6,30	3 (75.0%)
C	3 (7.14%)	5,8,22	2 (66.6%)
D	4 (11.11%)	4,6,9,10	4 (100.0%)

Table 3: Surgical complications among 4 residents.

Complication	A (n=40)	B (n=41)	C (n=42)	D (n=36)	Total (n=159)
Recurrence	8 (20.00%)	4 (9.75%)	3 (7.14%)	4 (11.11%)	19 (11.94%)
Dellen	-	-	1 (2.38%)	-	1 (0.63%)
Tenon prolapse	-	1 (2.43%)	-	-	1 (0.63%)
Corneal scar	2 (5.00%)	1 (2.43%)	2 (4.76%)	1 (2.77%)	6 (3.77%)
Graft retraction	1 (2.50%)	-	-	-	1 (0.63%)
Epithelial cyst	1 (2.50%)	-	-	-	1 (0.63%)
Pterygium granuloma	-	-	1 (2.38%)	-	1 (0.63%)

considerable amount of surgery, the variable factors between the surgeons will reduce thereafter.

The skill development of pterygium surgery may be assessed by monitoring recurrent pterygium as mentioned previously. The decreased operating time as the number of patients indicate increased skills in surgery. The incidence of recurrent pterygium can result in the quality of the operation based on this experience. However this complication may not be the only surrogate marker for skill development of the surgery due to many confounding factors. Whether it is patient related factors such as the age of the patient, ethnicity or even the status of the pterygium preoperatively (size, amount, inflamed severity) as well as the behavior of daily UV light exposure. In addition the recurrent pterygium may be caused by the surgeon who performed the surgery owing to variation in surgical experience and surgical technique.

Farrah et al. found recurrent pterygium following primary pterygium excision with conjunctival autograft transplantation (CAG) performed by trainees and consultants 19.4% and 6.8% respectively.[28] Also Kositpipat K. et al. published a prospective study reporting recurrent pterygium after primary pterygium excision with conjunctival autograft transplantation 9.7% and 4.8% respectively.[29] The following study showed the lower incidence rate of recurrence in experienced surgeons. By the way there were no significantly difference between two groups in some studies.

Chalioulias et al. found no different results for primary pterygium removal with CAG of those performed by the consultants and trainees (26.3 and 24.3 %, respectively).[30] In our study the participating residents are considered as inexperienced surgeons with a recurrence rate of pterygium excision with amniotic membrane transplantation approximately 11.94%. All of which occur within the first 6 months after pterygium surgery. Previous study as mentioned above conducted about the rate of recurrent pterygium by conjunctival graft comparing to amniotic membrane transplantation had result similarly to our study. By analyzing the sequence of recurrent pterygium patients for each resident (the average amount of pterygium case per each resident is 37.75), most recurrent pterygium occurs within the first 10 patients from each ophthalmology resident. As the number of cases increase so does the decline in recurrent rate reflecting the affect to learning curve to the surgeon experience.

Our study was prospectively designed to minimize confounding factors. The result is then evaluated by the author as an independent observer. This study is a part of routine to research and it can further be used to develop ophthalmology residency training programs. The improvement point of this research is that the number of patients of each resident should be increased to obtain an average operating time at a more stable level and it will represent precise learning curve and skill development bestowing confidence about the accuracy in assessment of the surgical skill development in ophthalmology residents.

Conclusion

Most ophthalmologists perform a lot of pterygium surgeries in clinical practice. Its frequency is the second only to cataract surgery. Due to the straight-forward nature of the surgery method combined with the complexity of hand-skills required, pterygium excision is widely used for residency training as a basic procedure for microsurgery. The learning curve requires an achievable amount of time suitable for skill development within a training program. Possible complications such as recurrent pterygium is also acceptable for an inexperienced surgeon. Re-operation causes considerably less morbidity compared to other eye surgeries. Overall pterygium excision is suitable for ophthalmology residency training, but nevertheless the surgery should be conducted and monitored by experienced ophthalmologist to minimize the risk to the patients.

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Macular edema after cataract surgery in diabetic patients evaluated by spectral domain OCT at Thammasat eye center

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Objective: To estimate the incidence of postoperative development of macular edema among diabetic patients with and without diabetic retinopathy. A comparative study of central macular thickness was performed on this population before and after uncomplicated cataract surgery.

Methods: Forty-two diabetic patients with no diabetic retinopathy (no DR) and 23 diabetic patients with diabetic retinopathy (DR) that underwent phacoemulsification with intraocular lens implantation were enrolled in this study from March 2017 to May 2018. Central macular thickness (CMT) was measured with spectral domain optical coherence tomography (OCT). These parameters were recorded before and four-weeks after cataract surgery then analyzed using descriptive statistics.

Results: 65 patients consisted of 40 males (61.54%) and 25 females (38.46%). Mean age was 67.01 ± 8.12 years. All 65 patients had diabetes, of which 23 (35.38%) had diabetic retinopathy and 42 (64.62%) did not. Phacoemulsification with posterior chamber intraocular lens implantation were performed in all eyes. No serious intraoperative complications were found. Mean preoperative CMT were 230.10 ± 25.25 and 233.78 ± 28.13 µm in the no DR and DR group respectively (P= 0.705). Mean postoperative CMT were 235.67 ± 27.59 and 239.04 ± 29.68 µm in the no DR and DR group respectively (P= 0.676). Mean CMT increased over the preoperative study 5.57 ± 12.28 µm (2.40%) in the no DR group and 5.26 ± 7.67 µm (3.28 %) in the DR group. The incidence of all postoperative macular edema on spectral domain OCT (CMT > 300 µm) was 1.54%.

Conclusion: Central macular thickness in diabetic patients measured by spectral domain OCT increase after uncomplicated phacoemulsification at 4 weeks in both groups but there is no statistically significant difference between the no DR and DR group.

Conflicts of interest: The authors report no conflicts of interest.

Keywords: macular edema, spectral domain OCT, central macular thickness, phacoemulsification, diabetic retinopathy

Ethics: This study was approved for ethical research in human with the human research ethics committee of Thammasat University, Thailand (Research ID: MTU-EC-OP-6-016/60)

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Introduction

Cataract is a leading global cause of blindness and cataract surgery is also one of the most common surgical procedures performed worldwide.[1] Pseudophakic

macular edema occurs commonly after cataract surgery, even in the absence of risk factors and complications.[2] The incidence of pseudophakic macular edema in previous studies varies between 0.20% to 20%.[3] In diabetic patients, postoperative macular edema is a complex and frequent encountered problem, especially in patients with preexisting diabetic retinopathy. Some investigators also found an increased progression of retinopathy and a higher incidence of macular edema after cataract surgery.[4-6]

Several studies made attempts to identify the risk factors of postoperative macular edema in diabetic eyes, though the exact cause of this phenomenon was still undetermined.[7] Some studies found that diabetic eyes had a high incidence of increased center macular thickness on optical coherence tomography (OCT) after cataract surgery especially in eyes with a history or presence of diabetic macular edema (DME) before surgery.[7,8] Spectral domain OCT is useful for retinal thickness monitoring quantitatively and qualitatively. It is proven to be a sensitive diagnostic test for the early detection of macular thickening in diabetic patients.[9] Our study is designed to assess the quantitative change of macula in diabetic eyes after cataract surgery using spectral domain OCT to estimate the incidence of macular edema after surgery in diabetic eyes comparing between no DR and DR group. In eyes with diabetic retinopathy, the blood retinal barrier is often impaired to a variable degree, which may cause eyes to be more prone to developing postoperative macular edema depending on the disease severity, duration and presence of pre-existing macular edema.[8]

Materials and Methods

A prospective cohort study was conducted at Thammasat eye center from March 2017 to May 2018. Forty-two diabetic patients with no DR and 23 diabetic patients with DR who underwent phacoemulsification with intraocular lens implantation were enrolled.

Inclusion criteria

1.Eyes diagnosed cataract in diabetic patient by a consultant level ophthalmologist.
2.Patients aged between 30 to 80 years old.
3.Patients informed and consented to participate in this study.
4.Patients able to attend follow-up at least 4 weeks postoperatively.

Exclusion criteria

1.Eyes with presence of macular edema within 3 months before surgery.
2.Eyes with previous macular scar, ocular trauma or other retinal diseases.
3.Eyes with history of previous intraocular surgery.
4.Patients with intraoperative or postoperative complications such as ruptured posterior capsule or endophthalmitis.
5.Patients unable to consent for follow up according to study protocol.

This study had been approved by the ethics committee of Thammasat University, Thailand. Informed consents were obtained from all patients. The authors verified that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during this research, adhering to the tenets of the declaration of Helsinki.

Patients planned for cataract surgery were examined preoperatively and at 4 weeks after surgery. Preoperative and postoperative examination included visual acuity using a Snellen chart, slit-lamp biomicroscopy, fundus examination (diabetic retinopathy graded by ETDRS). Central macular thickness were measured by spectral domain OCT using commercially available equipment (Cirrus HD-OCT, Carl Zeiss Meditec, Dublin, CA, USA). Only eyes with a confirmed absence of macular

edema before surgery were enrolled. Eyes with central subfield thickness by OCT more than 300 μm were excluded. Cataract surgeries in this study were performed by multiple surgeons with similar technique. Topical NSAIDS was prescribed preoperatively. Temporal clear cornea incision was made, and continuous anterior curvilinear capsulorhexis was performed. For cataract surgery, phacoemulsification equipment "Centurion" (Alcon Laboratories Inc., Fort Worth, TX, USA) was used in this study. Lens nuclei was divided by chopper, then phacoemulsification and cortical aspiration were performed. After that, acrylic foldable intraocular lens was inserted into the capsular bag. Steroid and antibiotic eye drops were prescribed postoperatively and adjusted by individual surgeons upon routine follow up depending on postoperative inflamed grading. The change of central macular thickness recorded before and four-week after the cataract surgery were analyzed using descriptive statistics.

Results

In this study, 65 diabetic patients joined to have cataract surgery. The average age of patient was 67.09 ± 8.12 years old. Of the 65 patients, 40 patients (61.54%) were male and 25 patients (38.46%) were female. Laterality was 31 (47.69%) on the right and 34 (52.31%) on the left eye. Overall the data on age, gender and laterality distribution did not show statistically difference. Forty-two diabetic patients had no DR while 23 diabetic patients had DR. The baseline patient characteristics of both groups are shown in table 1. Among the DR group, there were 4 subgroups: 18 (78.26%) mild non-proliferative diabetic retinopathy patients, 3 (13.04%) moderate non-proliferative diabetic retinopathy patients, 1 (4.34%) severe non-proliferative diabetic retinopathy patient and 1 (4.34%) very severe non-proliferative diabetic retinopathy patient were shown in table 2. All eyes had no macular edema before surgery. Before surgery, mean preoperative central macular thickness by spectral

Table 1: Baseline demographic characteristics in the no DR and DR group.

Patient Characteristics	no DR group (n=42)	DR group (n=23)	*P*
Age (years)	67.62 ± 7.93	66.13 ± 8.24	0.784
Gender	Male 25 (38.46%) Female 17 (26.15%)	Male 15 (23.07%) Female 8 (12.31%)	0.326
Laterality	Right 18 (27.69%) Left 24 (36.93%)	Right 13 (20.00%) Left 10 (15.38%)	0.854
DR staging	No DR 42 (64.62%)	DR 23 (35.38%)	1.000

Table 2: The proportion of diabetic retinopathy patients in different stages.

NPDR staging	mild NPDR	moderate NPDR	severe NPDR	very severe NPDR
Number (%)	18 (78.26%)	3 (13.04%)	1 (4.34%)	1 (4.34%)

* NPDR is non-proliferative diabetic retinopathy

Table 3: Baseline preoperative central macula thickness between the no DR and DR group.

Patient characteristics (preoperative)	no DR group (n=42)		DR group (n=23)		*P*
	Mean	SD	Mean	SD	
Preoperative CMT (μm)	230.10	25.25	233.78	28.13	0.705
Duration from surgery to postoperative OCT testing (days)	32.81	11.22	35.70	16.88	0.801

Table 4: Difference in postoperative central macula thickness between the no DR and DR group.

Patient characteristics (postoperative)	no DR group (n=42)		DR group (n=23)		*P*
	Mean	SD	Mean	SD	
Postoperative CMT (μm)	235.67	27.59	239.04	29.68	0.676
Change of CMT pre and post operation (μm)	5.57	12.28	5.26	7.67	0.456

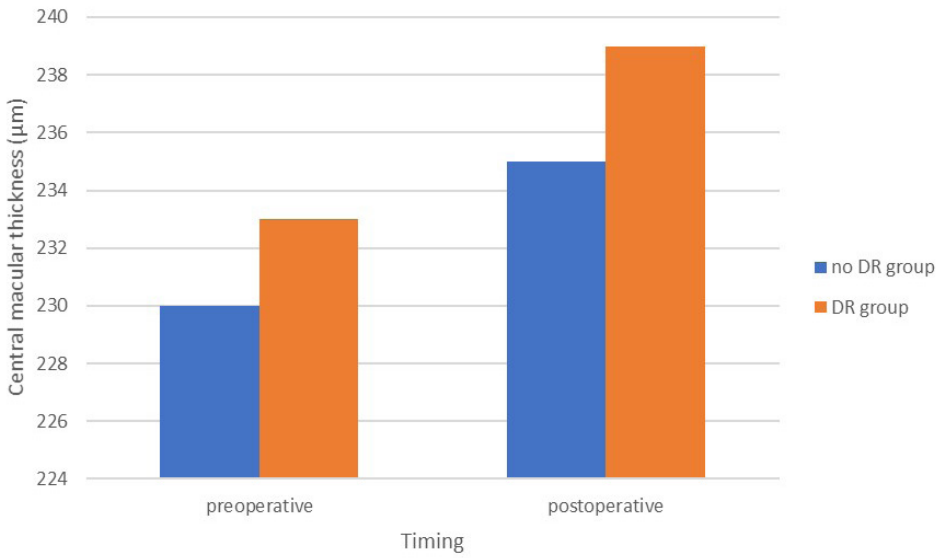

Figure 1: Comparison of preoperative and postoperative central macular thickness between no DR and DR group.

domain OCT was 230.10 ± 25.25 μm in the no DR group and 233.78 ± 28.13 μm in the DR group (P = 0.705) shown in table 3. There was no difference in preoperative CMT between the two groups.

Of all the eyes in this study, cataract surgery was performed using phacoemulsification with posterior chamber intraocular lens implantation. No serious intraoperative complications were found obviously. After cataract surgery, mean duration from surgery date to postoperative OCT testing were 32.81 ± 11.22 and 35.70 ± 16.88 days in the no DR and DR group respectively. Table 4 showed the comparison of postoperative CMT between the no DR and DR group. There was no significant difference in mean postoperative CMT (P = 0.676). Between the preoperative and postoperative group, mean change of CMT was also no significant difference (P = 0.456).

Central macular thickness increased over the preoperative study approximately 2.40% in the no DR group and 3.28% in the DR group as shown in Figure 1. Finally, the incidence of all central macular edema on postoperative OCT (CMT > 300 μm) was 1.54%.

Discussion

This study investigates the change of CMT evaluated by spectral domain OCT before and after cataract surgery in both diabetic patient groups (no DR and DR group). The results reveal an increase in CMT found at 4 weeks postoperatively in both groups (P = 0.456). The increasing of CMT following cataract surgery in diabetic patients depends on both the presence with and without diabetic retinopathy preoperatively. These factors possibly aggravate macular thickness after cataract surgery. Furthermore, many studies revealed increasing of CMT postoperatively. Pollack et al. found that mean central macular thickness increased approximately 21.00 μm after surgery.[10] The significant increase of CMT was detected by spectral domain OCT in their study.[11]

Past studies have defined the incidence of macular edema after cataract surgery by fundus fluorescein angiography, but in this study today define the incidence of macular edema by spectral domain OCT. The cutoff to define macular edema varied in many studies. Some concluded that an increase of central macular thickness of 30% was a useful criteria because it was the point of experienced significant loss of vision.[6] Following this cutoff point, the incidence of macular edema in this study is null. Typically, macular edema in diabetic patients after cataract surgery cannot be clearly attributed to a cause, whether it is as a result of diabetic retinopathy, or cases that developed cystoid macular edema (CME). In our study, every case receives non-steroidal anti-inflammatory drugs (NSAIDS) eye drops to prevent CME before the operation, which may reduce the incidence of macular edema. This finding is similar to many studies, suggesting that the macular status in diabetic patient is still good in the first 4 weeks after phacoemulsification.[8,12] The small sample size in our study may cause our result to be insignificant. In contrast to the study of Stephen et al. which demonstrated that 22% of diabetic patients developed a 30% increase in central macular thickness at 4 weeks after uncomplicated phacoemulsification.[6] So all of the results of these studies were not quite the same.

Upon comparing the change in CMT between the no DR and DR group after cataract surgery, we found that there were no statistically significant differences in CMT between both groups. Our result is similar to the study by Wang et al.[8] and Flesner et al.[13] who concluded that the level of severity of DR did not contribute to the risk for developing macular edema after cataract surgery in diabetic patients. In our study, the severity of diabetic retinopathy group

is mostly mild non-proliferative diabetic retinopathy (mild NPDR), so this may be a contributing factor towards our statistically insignificant result. Other studies comparing between 3 groups consisting of no DR, NPDR and proliferative diabetic retinopathy (PDR) group should be brought to study more. A study by Kim et al. found that different levels of preoperative diabetic retinopathy were correlated with increased postoperative central macular thickness.[6] The eyes in their study with moderate NPDR, severe NPDR, very severe NPDR and PDR developed thickening of macula much more frequent than eyes with no DR.[6] Back to our study, this duration of the collected data is limited to approximately 4 weeks after surgery, so we could not detect late progression of macular edema. Finally, the author also has the opinion that preoperative cataract severity factors such as lens graded opacity and the difficulty of phacoemulsification can affect central macular thickening postoperatively.

Conclusion

Mean change of CMT measured by OCT in diabetic patients of this study increased by 2.40% in the no DR group and 3.28% in the DR group after uncomplicated cataract phacoemulsification at 4 weeks, but there are no statistically significant difference of macular thickness between the preoperative and postoperative group. Also there are no statistically significant difference in change of CMT after cataract surgery between the no DR and DR group. The incidence of macular edema after cataract surgery measured by spectral domain OCT (CMT > 300μm) is 1.54%, which was found only in the DR group. Uncomplicated phacoemulsification is safe for postoperative macular edema development in patients with mild degree of diabetic retinopathy.

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The association between contact lens wear and the meibomian gland dysfunction in ophthalmology department, Thammasat hospital, Pathum Thani, Thailand

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Purpose: To determine the prevalence of Meibomian gland dysfunction (MGD) in contact lens wearers and the effect of different modalities of contact lens (CL) on parameters related to MGD in. Thammasat hospital, Pathum Thani province.

Methods: Cross-sectional study. 75 contact lens wearer subjects (ages 20-50 years old). The subjects' health history and symptoms were assessed using questionnaire. The assessment of MGD and dry eye symptoms was conducted by a self-reported ocular symptom using ocular surface disease index (OSDI).

Results: There was a significant association between the severity of MGD and artificial tear used, participants who used artificial tear have less severity of MGD 1.36 compare to non-used group 1.63 ($P = 0.01$). It was found that severity of MGD had a significant correlation with color of CL ($P = 0.023$). The tinted and big eye CL seemed to produce higher degree of MGD comparing to clear CL, suggesting that CL material was significantly related to severity of MGD. Short time of CL wear per day seems to have lower severity of MGD.

Conclusions: MGD was found to be common in contact lens wearers' subjects in Pathum Thani province, up to 74.7%. The severity of MGD had significant correlation with CL material.

Conflicts of interest: The authors report no conflicts of interest.

Keywords: contact lens wear, meibomian gland dysfunction, ocular surface disease index, Pathum Thani Province

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Introduction

Contact lenses have become very popular, not only for its use to correct a refractive error but also widely used in cosmetic way. However, wearing contact lens for a long period of time could lead to the development of many complications, such as dry eye, corneal surface abnormalities (corneal abrasion) and allergic conjunctivitis or infection. Among these, one of the most common complications observed is dry eye. Dry eye disease (DED) is characterized as either aqueous-deficit dry eye (ADDE) or evaporative dry eye (EDE).[1] It is a common, complex disease that causes symptoms of eye discomfort, change in visual acuity and tear film instability with potential damage to the ocular surface. Dry eye disease normally occurs due to an abnormality of

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tear film production (quality) or quantity of tear film components. Tear film has 3 layers; the innermost is mucin layer, secreted from goblet cell. The second layer is aqueous layer which secreted from lacrimal gland. The outermost is lipid layer which secreted from Meibomian gland. It is well recognized that defective formation of the lipid layer of tear film due to Meibomian gland dysfunction (MGD) could lead to evaporative dry eye disease (EDE).[2] This is consistent with the finding that MGD is a major cause of EDE.[3-5] The key signs of MGD include MG dropout, altered MG secretion, and changes in the lid morphology.[6]

It has been estimated that there are at least 140 million contact lens (CL) wearers worldwide.[7] Approximately 50% of CL wearers reported dry eye symptoms.[8-11] Moreover, it was found that CL wearers present with dry eye symptoms 12 times higher than those who do not wear contact lens, and 5 times higher compare to those who wear glasses.[12] Many studies have examined the association between CL wear and MGD, suggesting that lens wear produced adverse changes in MG function. The prevalence of MGD and CL wearers in several studies was about 22-37%.[13] A strong correlation between Meibomian gland dysfunction (MGD) and contact lens wearer in Asian people was reported.[2]

Of note, wearing contact lens can cause MGD due to an obstruction of the glands by kerotoic plugs. A consequence of the Meibomian gland obstruction could lead to bacterial aggregation and inflammation that resulting in reduced tear film quality[14], increased osmolality and easily to evaporate.[3] In addition, the number of Meibomian glands was reported to decrease concurrent with the duration of contact lens wearers.[15] However, the association between CL wear and MGD remains inconclusive. The discrepancy could be due to the limitations in the study designs and several parameters involved including duration of CL wear, lifestyle and environmental factors. However, the prevalence of MGD in correlation with type and duration of contact lens wear has not been examined in the Thai population. Due to the raising concerns about the safety of their long-term CL use, this study was performed to evaluate the effect of different modalities of contact lens on parameter related to MGD. The results obtained from this study will provide safe and effective recommendation for contact lens wearer.

Materials and methods

Study population

The study comprised of 150 eyes from 75 contact lens wearer subjects with the ages ranged from 20 to 50 years who came to Ophthalmology department, Thammasat hospital. Subjects were excluded from the study if they have signs of acute eye infections, lid abnormalities, or systemic diseases that might affect dry eye disease such as Sjogren's syndrome. Moreover, the subjects using topical medications for instance, topical anti-glaucoma drug that may interfere with ocular surface diseases were also excluded but those using artificial tear were allowed to participate. An informed consent was obtained from the subjects prior to an examination. The subjects were requested to remove contact lens before examination.

The study design and protocols were approved by ethic committee of Thammasat University, Thailand (MTU-EC-OP-0-146/58).

We assessed the subjects' health history and symptoms using structured questionnaire. It included gender, age, comorbid diseases, current medication(s), artificial tear used, past history of ophthalmic surgery, details of contact lens; type, color, daily or monthly, duration of CL use, and lens brand. In addition, a self-reported ocular symptom using the Ocular Surface Disease

Index (OSDI) was also included in the questionnaire.[19]

An examination was performed in the following order: visual acuity, slit-lamp examination of lid margin, Meibomian gland's expression and function, tear break-up time and corneal staining.

After best-corrected visual acuity was recorded, subjects were examined in front of slit-lamp. The lid margin was examined and the score was graded as 1 (normal lid margin), 2 (irregular lid margin), 3 (plugging and vascularity) and 4 (drop out and displacement). Its debris was graded as 0 (none), 1 (1-5 crusts), 2 (6-10 crusts), and 3 (>10 crusts). In addition, the lid margin redness also graded as 4-point categorical scale (none, pink, light red and bright red) (Table 1).

Meibomian gland secretion was assessed in each of 8 glands at the central third of lower lid on a 0-3 scale for each gland (Table 2). Light digital pressure was applied constantly at both lower lids to examine Meibomian gland's secretion characteristics. Conjunctiva was examined and injection score was also assessed(Table2).

Tear film break-up time was measured by placing a fluorescein-impregnated strip in the lateral part of inferior fornix. Each subject was asked to blink several times. Cobalt blue light was then illuminated and the time before the corneal dry spot appeared in the stained tear film was recorded as the tear film break-up time. Subsequently, corneal staining was evaluated after reapplying of fluorescein staining under cobalt blue illumination. Appearance of corneal staining was recorded and graded on a 1-5 scale (none, minimal, mild, moderate, marked staining) as references from TFOS international workshop on Meibomian gland dysfunction[16] (Table 2).

Statistical Analysis

All statistical analyses were performed using SPSS. The data were presented as percentage (%) of the total subjects or mean values ± SD. The data were analyzed using one way ANOVA followed by LSD test to draw comparison between MGD and related variables of the subjects and that of the contact lens. A $P < 0.05$ was considered to be statistically significant in all analyses.

Results

The clinical characteristics of the 75 subjects whom were recruited and evaluated at Thammasart hospital between September [1], 2016 and April 30, 2017 are summarized in Table 3. The mean age was 26.14 (SD 7.23) years (range, 19-46 years), and 82.7% were woman. The 20 % of subjects has allergy, 74.7% has no underlying disease and 5.3% others. Moreover, the current medications used that might affect dry eye syndrome were shown in Table 3. It was found that most of the subjects have no drug history and only 13.3% used antihistamine drug. Subjects with history of Roaccutane, antihistamine and hormone used did not shown statistically higher incidence of MGD. Of note, about 70% of subjects used artificial tear as a single dose unit or monthly artificial tear. This may indirectly reflect dry eye symptom of CL wearers. In subjects with artificial tear used, the most frequency used is 3 times a day (16.0%). 96% of subjects had no previous ophthalmic surgery. As shown in Figure 1A, most of the subjects wear soft contact lens (96.0%) and only 3% wear rigid ones. Monthly contact lenses were the most commonly used by about 80.0% (figure 1C). Interestingly, there were varieties of CL used (Figure 1B). Those include clear lens (68%), tinted lens, lens that have had a dye incorporated into the lens material (13.3%), and big eye contact lens, lens with diameter larger than normal (2.7%). The rest wear more than one type. The duration of hours wearing contact lens of subjects each day were reported in various ranges as followed; less than 6 hours (4%), 6-8 hours (17.3%), [9-10] hours (37.4 %),

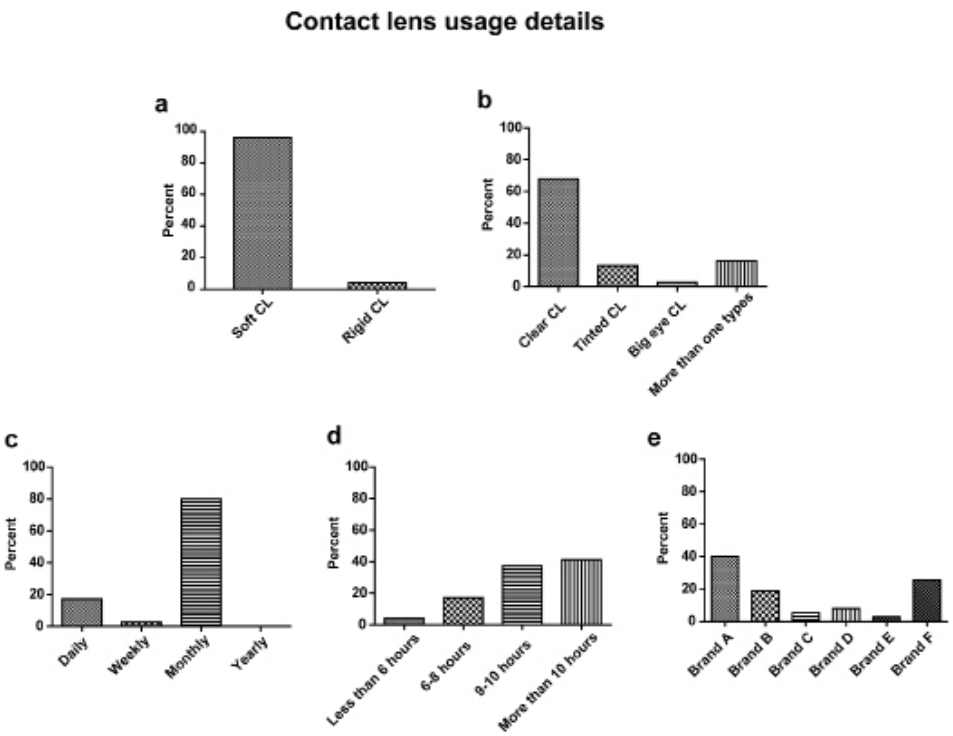

Figure 1: Contact lens usage details. A: type of CL, B: color of CL, C: CL wearing time, D: hours of wearing per day, E: Brand of CL

and more than 10 hours (41.3%) (Figure 1D). The mean duration of contact lens wear was 70.3 months (range 1-240 months, SD 57.51). The percentage of contact lens brands by which the subjects used was shown in Figure 1F.

Self-reported ocular symptoms or ocular surface disease index (OSDI) were measured as shown in Figure 2 with the result of mean value 24.37 (range 1-69, SD 15.78). The majority of subjects (86.7%) have best-corrected visual acuity at 20/20. In this study the prevalence of MGD in contact lens users were 74.7% (Grade 2) (Table 7). Similar to previous studies, the prevalence of dry eyes were also high in contact lens wearers. The severity of MGD was evaluated and graded using many parameters as shown in Table 2 and the results were shown in Figures 3, 4 and 5. There were the association between the severity of MGD and artificial tear used, participants who used artificial tear have less severity of MGD 1.36 compare to non-used group 1.63 ($P < 0.01$) (Figure 5D). Female participants have average severity of MGD at 1.54 and male participants at 1.48 ($P = 0.618$). Interestingly, there

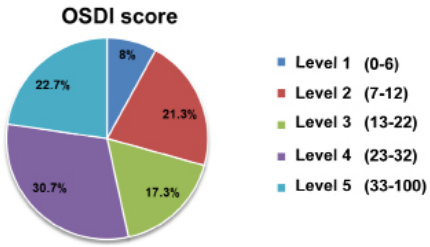

Figure 2: Distribution of OSDI score with the range between 1-69, mean value ± SD = 24.37 ± 15.78

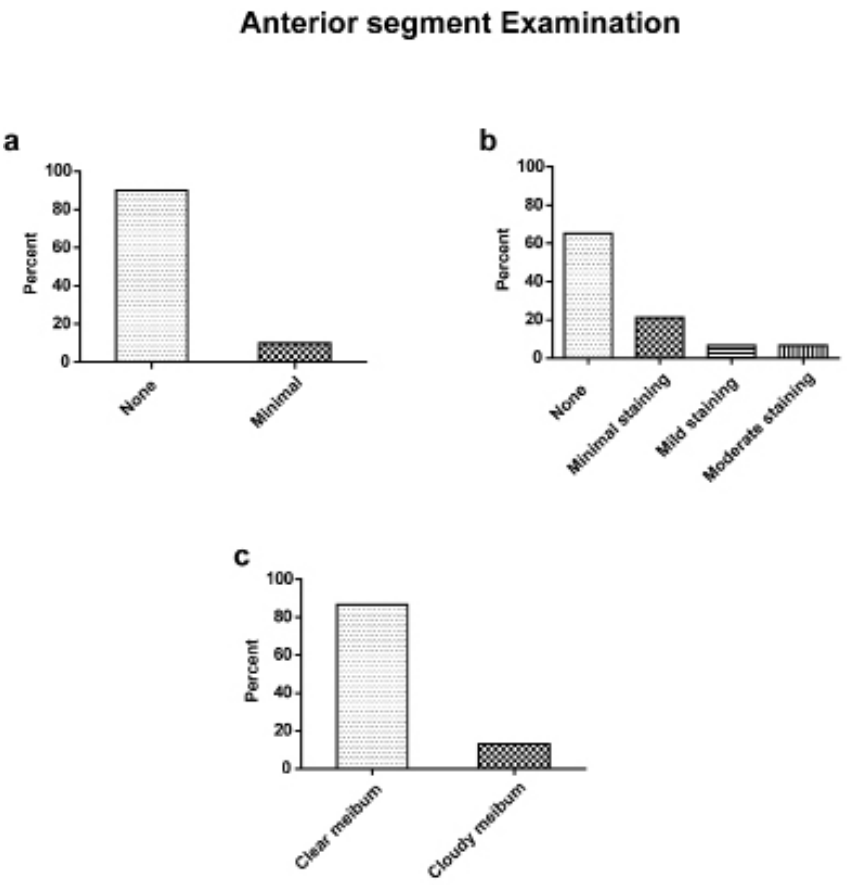

Figure 3: Anterior segment examinations. a Conjunctival injection score, b Corneal fluoresceine staining, c Meibomian gland quality grading

was no significant different in severity of MGD between age groups (P = 0.304). The severity of MGD in soft contact lens users are 1.53 and rigid contact lens users are 1.63 (P = 0.683). The severity of MGD in subjects who wear clear contact lens, tinted contact lens, big eye contact lens and others were at 1.53, 1.80, 1.83 and 1.29, respectively. It was noteworthy that the severity of MDG had significant correlation with color of CL (P <0.023) (Figure 6). The tinted and big eye CL seemed to produce higher degree of MGD severity comparing to clear CL, suggesting that CL material was significantly related to severity of MGD.

CL wearing time; daily, weekly and monthly, had an average MGD of 1.50, 1.56 and 1.54 respectively (P = 0.943). Notably, the hours of contact lens wear per day

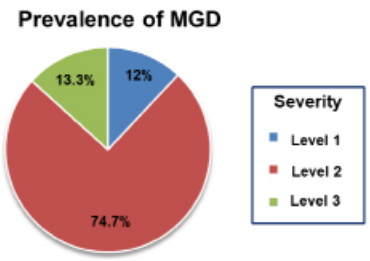

Figure 4: Prevalence of MGD with the range 1-3, mean value ± SD = 1.53 ± 0.42

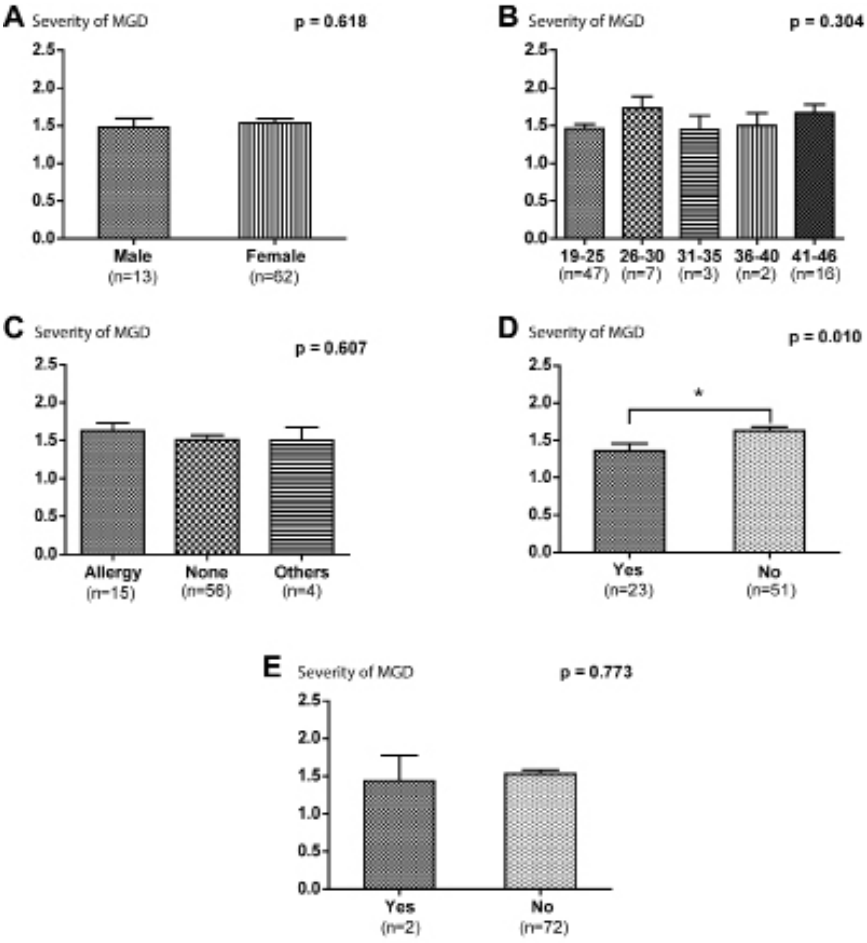

Figure 5: Severity of MGD compare with personal factors. A: Sex, B: Age, C: Underlying disease,D: Artificial tear use, E: Ocular surgery

seemed to have slightly effect on severity of MGD; more than 6 hours (1.28), 6-8 hours (1.44), 9-10 hours (1.52) and more than hours (1.57) (P = 0.676). Duration of CL wearing has no significant effect on severity of MGD (P = 0.687). These findings indicated that CL wearing time, hours of wearing per day, duration of lens wear and brands of CL were not significant factors related to MGD. However, short time of CL wear per day seems to have lower MGD.

In this study, we found that an increase in duration of CL wear seemed to have slightly effect on TBUT. As the duration of CL wearing is longer, the more potential of an increasing in TBUT score may appear (the more score is less TBUT). This reflects the effect of duration of CL wear on severity of dry eye and also the severity of MGD (Figure 7).

Of note, the lid margin score that reflects the function of MG had tendency to increase with increased wearing duration (Figure 8). Due to the small number of subjects who wore CL at longer duration, this makes it difficult to draw solid conclusion

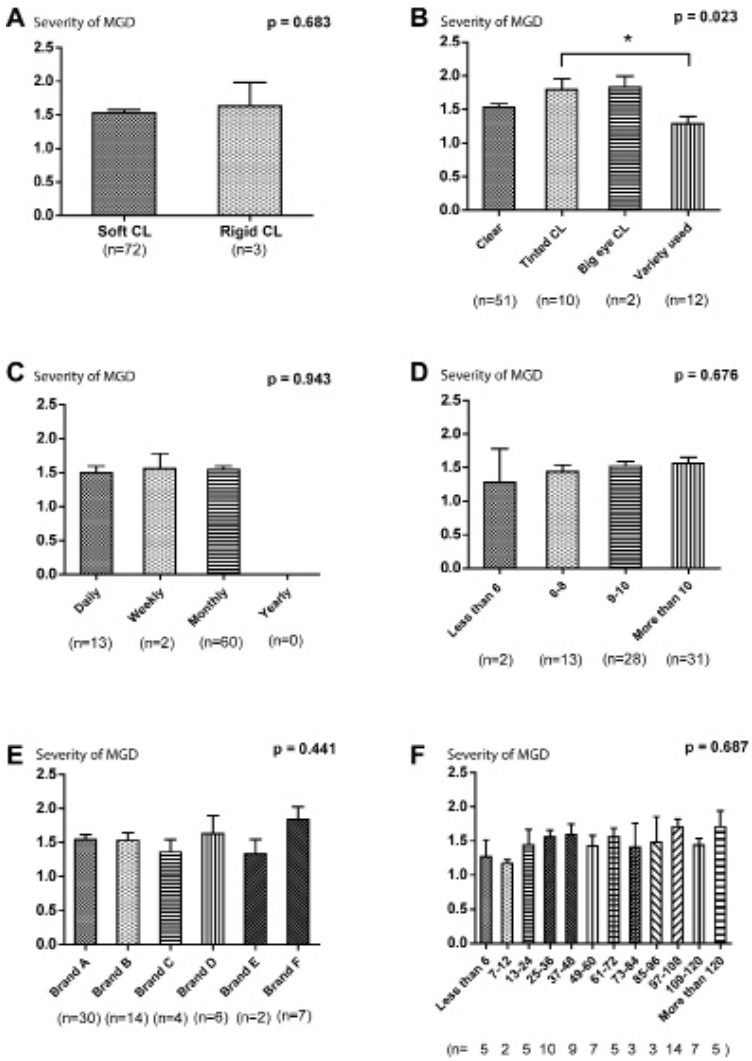

Figure 6: Severity of MGD in correlation with contact lens factors. a Type of CL, b Color of CL, c CL wearing time, d Hours of wearing per days, e Duration of CL use (months)

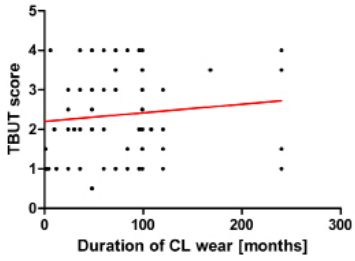

Figure 7: Scatter plot showing correlations between TBUT and duration of CL wearers in 75 subjects

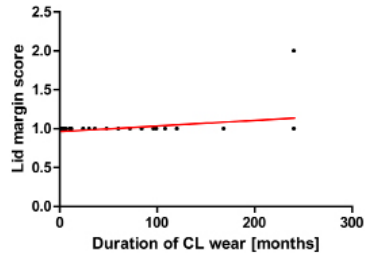

Figure 8: Scatter plot correlations between the lid margin score and duration of CL wearers in 75 subjects

on this assumption. However, it was likely that duration of CL wear might be an independent predictor of lid margin abnormalities.

Discussion

MGD is a multifactorial disease which is a major cause of EDE. It is commonly characterized by terminal duct obstruction and changes of meibum secretion. The proposed mechanism of MG obstruction is likely to be due to aggregation of desquamated epithelial cells into keratotic clusters that block the meibomian duct[13]. Without high quality meibum, the tear will evaporate quickly causing dry eye. It has been stated that 50% of CL wearers get dry eyes which making over 75% drop out of CL wearing because of dry eye[13]. To maintain their correct shape, contact lens need to be well hydrated. Thus, under certain conditions it is possible that CL could soak up tears on the ocular surface leading to dry eye. Although, the leading cause of dry eye symptom for CL wearers has been suggested to be due to MGD. The extent by which CL wear contributes to MGD is still unclear. In contrast, the lack of association between CL wear and MGD was also reported.[17] Since the high prevalence of MGD in Asian population has been reported, it is of interest to investigate the relationship between CL wear and various signs involving MGD inPathum Thani province. Our study found that MGD was common in Thai contact lens users, up to 74.7% in the study group. This is consistent with several previous studies showing that MGD was observed in contact lens used.[18]

Of note, MGD is likely to include multiple interactions between endogenous and exogenous factors. We then investigated the effect of different modalities of contact lens on parameters related to MGD. Concerning the type of CL, the data obtained from our study showing that rigid contact lens users had no significant different in severity of MGD compare to that of soft contact lens users. In fact, this finding was similar to that reported in previous study. However, our data was not strong enough evidence to make solid conclusion concerning the effect of the rigid contact on MGD due to the low number of subjects in this group (n=3). Therefore, higher numbers of subjects in this group is needed. Notably, other factors have been found to correlate well with the prevalence and severity of MGD in the present study. The different color of contact lens used was found to have significant different in severity of MGD (P = 0.023). Subjects, who wear big eye contact lens tended to have more severe MGD than that of the others with the mean value of 1.83. The one using variety (combination) of contact lens has less severity of MGD compare to tinted contact lens, 1.29 vs. 1.80 (P = 0.004). There was a report that duration of contact lens wear associated with meiboscore which represents severity of MGD. This is consistent with our study showing that the longer hours of contact lens wearing, the more possibility of MGD observed. In addition, there was a correlation between severity of MGD and artificial tear used. This finding is consistent with the results previously reported by Machalinska et al.[18].

In parallel, there were a few studies demonstrated the prevalence of lid margin and conjunctival abnormalities in CL wearers.[18] Of note, only a few weeks of daily CL wear a significant increase in the IL-6 tear film concentration was found despite normal conjunctival and corneal cell morphology. These data suggested that CL wear may affect ocular homeostasis and induce tear film inflammation.[18] Along the line, it has been proposed that CL wear may induce chronic irritation of MGs through conjunctiva which causes changes in MG function and meibum quality.[18] Our results are in agreement with this notion; we found changes in meibum quality and likelihood

of lid margin abnormality in CL wear (Figure 8). The longer period of CL wear may be required to see significant increase in lid margin abnormality in CL wear. The previous study has shown that lid margin abnormality start to observe after 10 year of CL wear.[18]

In addition, determination the association between CL wear and dry eye status using TBUT and conjunctival staining showed no significant correlation among these parameters. This might be explained by high frequency of artificial tear use by CL users. It is noteworthy that the frequency of artificial tear use correlates with ocular symptom score. This factor may have some influence on the results of our study to some extent. Due to the fact that the subjects in our study group are considered to be a young age population and composed mostly female, it may not be representative of the whole Thai population of CL users. Moreover, the longitudinal study of CL wear on MGD should be performed to establish better understanding of the link between duration of CL wear and the severity of MGD manifestation.

In conclusion, we have shown the evidence that CL wear may predispose subject to MGD. The severity of MDG had significant correlation with CL material. The possibility of MGD is normally not investigated unless significant symptoms are developed. Therefore, the routinely MGD examination of CL wearers is recommended for early and effective management.

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Patients' barrier to adherence with glaucoma therapy experience: a qualitative research study

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Purpose: To explore the experiences of therapeutic glaucoma adherence in patients with glaucoma regarding the obstructive factors to adherence and its importance to health outcomes.

Methods: This qualitative study, purposive sampling, was used to recruit ten glaucoma patients. Data were collected from the outpatient ophthalmology clinic at Thammasat University Hospital between January and June 2017 using in-depth interviews along with observation and field records. Data were analyzed using content analysis.

Results: The main findings illustrated that adherence barriers with glaucoma therapy in patients with glaucoma were 1) lacking essential knowledge and 2) forgetfulness. Adherence is crucial to the overall general health of glaucoma patients because it helps them able to proper healthcare, resulting in better therapeutic outcomes and able to independent living.

Conclusion: The results present an understanding of specific obstacles to adherence to anti-glaucomatous therapy. Future research should focus on investigating methods by which primary education related glaucoma and nursing management should be delivered to patients with glaucoma, leading to preserve the remaining eyesight diminishes.

Conflict of interest: The authors declare no conflict of interests.

Keywords: Barrier to adherence, Experience, Patient with glaucoma, Qualitative research

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Introduction

Glaucoma is the second leading cause of blindness in Thailand and worldwide. It is a chronic, progressive, and asymptomatic disease. The condition is initially asymptomatic, whether an untreated process can result in gradual visual field loss and, eventually, blindness. Despite the condition being an "incurable disease," glaucoma is still treatable, and the primary objective of glaucoma therapy is to prevent progressive visual field loss, disability, and blindness.[1-2] Patient adherence has long been recognized as an essential factor in controlling glaucoma. If patients are not adherent to the therapeutic regimen, the patient exhibits higher IOPs and more advanced visual field loss. Then, the chance of preserving

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their remaining eyesight diminishes.[3-4] Several published studies in Southeast Asia suggest that medical adherence among glaucoma patients is inadequate, between 50% and 63.4%.[5-6] The nonadherence can be summarized as intentional and unintentional nonadherence. The prevalence of unintentional nonadherence may vary depending on the patient's age, forget, understanding of glaucomatous progression, motivation, and confidence in their doctor.[7-8] As healthcare providers, we need to recognize the noncompliance barriers in the viewpoint of glaucoma patients in their contexts.

Objective

To explore patients' experience in terms of barriers to adherence with glaucoma therapy regarding the barrier to adherence with glaucoma therapy and the importance of adherence to the health outcomes.

Method

This study used a qualitative approach. Purposive sampling was used to recruit ten glaucoma patients who met the following inclusion criteria: (a) patients who were diagnosed by ophthalmologists as glaucoma received at least 1 glaucoma drop for more than 3 months (b) able to communicate and understand Thai (c) consented to participate in this research. Exclusion criteria: (a) informants have acute glaucoma and (b) having other complications (e.g., cataract, uveitis, and eye trauma, etc.).

The primary research served as the instrument of data collection, along with the interview guidelines. The primary researcher used a memo note, reflexivity during data collection and data analysis.

In this study, the data collection method included: in-depth interviews, participation observation, and used field records. Interview times and places were arranged at the informants' convenience and ranged from 15-30 minutes. All informants allowed audio-taping of the interviews. Interviews were started with a general question (What is your goal when you receive glaucoma treatment?). The probing technique was used to gather more information. The second interview was conducted with eight informants. The third interview was requested from two informants for clarification and assurance that the data were completed.

Moreover, the primary researcher used field notes and participant observation. Data collection continued until the informants and data offered no new information were being repeated. Finally, all of the informants gave feedback about the accuracy of the interpretation of the findings. The study was approved by the Research Ethics Committee of Thammasat University (No. 3), Thammasat University, Thailand and was considered by the principle on International Conference on Harmonization-Good Clinical Practice, ID 031/2558.

This study adopted validity and reliability techniques based on Sandelowski's and Mayan's recommendation.[9-10] According to address validity, various data sources were used, a saturation of the data was carried out, and accuracy validation of the findings, between the primary researcher and informants, was conducted. To attain reliability, the principal investigator described her background to the informants, approached informant two to three timed for interviews, and used various data sources. Throughout the research process and analysis, the primary researcher asked for input from peers and the other members of the research team.

Data analysis was based on Dey's content analyses.[11]

Result

The findings can be categorized into two parts as (1) general data, and (2) the patient experience with therapeutic glaucoma adherence.

Part 1 general data

Informants consisted of ten patients with glaucoma, both male and female equally (50%); aged between 61 and 70 years old was the highest (40%). Half of them were married; seventy percent was graduated from an elementary school. Seventy percent of them were diagnosed with primary angle-closure glaucoma; time since diagnosed was between 1 and 10 years (80%). Two types of eye drop treated fifty percent of the informants; seventy percent of them (7 informants) used a hired motorcycle and a public transportation for ophthalmologist visiting (see table 1).

Part 2 the patient experience with therapeutic glaucoma adherence

The patient experience with glaucoma therapeutic adherence barriers are categorized as (1) therapeutic adherence barriers; and (2) the adherence importance to health outcomes as based on the following findings:

1. Therapeutic adherence barriers

Most of the key informants revealed that therapeutic adherence barriers could be concluded into two themes, as follows**:**

- Lacking essential knowledge

The key informants mentioned relating the therapeutic adherence barriers as (1) lacking essential knowledge; it meant that patients with glaucoma had inadequate information and understanding relating disease, treatment plan, and progressive disease outcomes, resulting in ignorance regarding proper healthcare. The following sentences supported this notion:

"Other patients I spoke with, they didn't use eye drops…they stored their eye drops and didn't use them…they didn't know their eyes will be blinded" (informant #2)

"Frankly…I didn't know…they [doctor/nurse] told me that I needed to take care of myself; I didn't do it…frankly speaking" (informant #6)

"I Did not know both disease and treatment…need to know from the beginning…If a doctor instructed from the beginning, I would have better cooperated" (informant #9)

According to essential knowledge or information, most key informants mentioned that they required knowledge relating disease, treatment plans, or continued modification of treatment plans, including progressive disease outcomes in cases of improper healthcare.

- Forgetfulness

Other therapeutic adherence barriers were forgetfulness; forgetful patients with glaucoma did not use medications as prescribed because of busy daily activities or work, including inconvenience to carry on medication due to proper medication storage (e.g., eyedrops requiring cold storage). The following sentences supported this notion:

"Forgot…my hands were sometimes dirty after work…after prolonged work; I then didn't want to make the medication dirty, or my wife sometimes dropped medication for me" (informant #4)

"Didn't always use eye drop…forgot sometimes…went out and didn't use eye drops…afraid of expired medication since a doctor told me that medication needed to be in a refrigerator all the time" (informant #10)

2. Adherence importance to health outcomes

However, most key informants presented that treatment cooperation is significant to health outcomes in patients with glaucoma because treatment adherence is related to the ability to proper healthcare, leading improve treatment outcomes and able to independent living. Appropriate healthcare resulted from having essential glaucoma information to apply for patients' participation and delayed disease progression through a discussion with related healthcare personals. The following statements supported this notion:

"I wish the doctor and I spoke about treatment…discussed the instructions … asked me if I any issues or informed me of some self-care tips sometimes …it would be good. A patient will understand, then properly follow instructions" (informant #5)

"I Want to take care of myself…actually; if I went to see a doctor from the beginning, it might be good" (informant #6)

Positive treatment outcomes result from proper performance according to instruction and treatment applying in daily life, leading to decreased incorporative treatment barriers, resulting in attaining medication as prescribed, for example, if a patient uses eye drop punctually, eye drops can control and reduce ocular pressure. Also, it can be immediately cured in case of complications, resulting in a higher treatment success rate or delayed disease progression. Consequently, the blindness rate is reduced. As stated by three key informants:

"Surely, supposed that he (a doctor) told me to use eye drops and use every 12 hrs., yet I cannot. It cannot reduce ocular pressure; it seems that visit to the doctor did not get me better" (informant #1)

"Importantly…glaucoma was very important to me since my first diagnosis, by myself…I confronted it. If I let it progress, it will give me acute pain and lead to operation and blindness…If I can control it, maybe I won't have blindness" (informant #3)

"Very important…firstly, a doctor would know regarding treatment outcomes improvement. Secondly, it provided benefit for patients…treatment outcomes would be rapidly improved" (informant #8)

Being capable of independent living results from adequate preservation of quality vision. Besides, patients with glaucoma can better interact with social networks and activities, leading to a happy life. The following statements supported this notion:

"Very important…important for my body…I want to improve…able to see… want to strong…able to go anywhere with the ability to see" (informant #7)

"If my eyes could not see anything… did not want to go anywhere…did not do anything…If eyes were blurred when went out, it was not funny. Others invited me to go out, but I didn't like to…unable to vision" (informant #2)

"If I could not see, a vision was not clear, led to transportation mistaking…everything was not clear, an accident would happen" (informant #4)

Discussion

The goal of this study was to study obstacles that patients with glaucoma experience when attempting to adherence to glaucoma regimens. The barriers to adherence for the patient with glaucoma are significant. Major reasons cited for nonadherence include lacking essential knowledge and forgetfulness. Lacking essential knowledge, Taylor, Galbraith, Mills[3] stated that patients generally want to be knowledgeable about glaucoma, healthcare providers are encouraged to inform patients about new medications that become available and help them understand each of their options, including laser and surgery. As Kosoko, Quigley, Vitale, Enger, Kerrigan, Tielsch[12] suggested that Poor understanding of the disease is also associated with poor adherence. Then, communication between providers and patients is a vital factor in adherence for glaucoma patients. Specifically, patients would like their providers to tell them about new/ alternate medications, and procedures have become available, and offer new ways to make their regiment easier.[3,13]

Almost half of these adherence obstacles reflected patient factors of forgetfulness. Taylor, Galbraith, Mills[3] also reported that patient forgetfulness was the number one reason for nonadherence. Forgetfulness is

included being away from home and the medication, inconvenient timing.[13]

In conclusion, this study, cause of nonadherence can be summarized as unintentional nonadherence in order to it occurred when the patient intends to take the treatment but is prevented from doing so by limitations in capacity and resource (forgetting, lack of essential knowledge). Most of the informant intend to treatment cooperate because they comprehend that glaucoma is a health condition which can be cured, and worse disease progression leading to blindness. Therefore, all informants mentioned that treatment cooperative is essential in case of attaining and comprehending necessary knowledge as needed, resulting in proper healthcare. Consequently, adequate healthcare leads to delay glaucoma progression, decrease optic nerve degeneration, maintain eyesight ability, resulting in independence daily living, and then they can typically interact with their social networks, leading to a better quality of life.

As Horn, Parham, Driscoll, Robinson[6] stated that unintentional nonadherence is common among chronic diseases. The most informants in this study (9 participants) that were interviewed expressed that they try to be adherent because they understand that they will go blind if their glaucoma progresses. However, glaucoma is a preventable cause of blindness if effective and successful treatment can be provided at the appropriate time.[14]

Conclusion

The results of this study demonstrate that significant barriers for patients with glaucoma are lacking essential knowledge, and forgetfulness. These barriers recognized and handled to assist health care providers in developing appropriate interventions and guidelines to optimize patient education regarding enhancing, and nursing care related to adherence, which leads to the change of preserving the remaining eyesight deterioration of patients.

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Photo Challenge: an educational innovation to stimulate effective learning in ophthalmology

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Background: The learning process in Ophthalmology emphasizes visual disease manifestations, which can be traced to aspects such as epidemiology, pathophysiology, clinical manifestations and management. However, contemporary teaching methods of lecturing are often insufficient for facilitating learning. Additionally, instructors find it difficult to evaluate the knowledge and understanding of students after lectures.

Method: Fifteen residents from three years of training were randomized and divided into five groups to compete in a quiz and discuss different aspects of the disease depicted in the photo. Qualified ophthalmologist instructors score the team's performance on quality and completion of discussion and provide feedback on the conformity, rationale and omissions of the discussion as a team.

Result: Ophthalmology residents participating in Photo Challenges favored the activity and benefited from engaging in the learning experiences as well as being given opportunities to practice clinical thinking processes by verbally approaching the clinical diagnosis from important findings and management of the disease. Instructors are able to assess their students' degree of success in learning outcomes and provide instant feedback.

Conclusion: Photo Challenge is an educational innovation is suitable for Ophthalmology learning and is effective for students to achieve learning outcomes as well as gain straightforward assessment from instructors. This teaching method can also be applicable to other studies where photographs are an important element in the learning process.

Keyword: Photo Challenge, medical education, educational innovation

Conflicts of interest: The authors report no conflicts of interest.

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Introduction

The learning process in Ophthalmology emphasizes visual disease manifestations, which can be traced to aspects such as epidemiology, pathophysiology, clinical manifestations and management. Clinical Images are considered to be efficient tools in medical education and enhance clinical diagnosis skills.[1,2] It has also been published that tests promote better retention of information and feedback is crucial to learning from tests.[3] However, contemporary teaching methods of lecturing are often insufficient for facilitating learning.[4] Additionally, instructors find it difficult to evaluate the knowledge and understanding of students after lectures.

Photo Challenge is an activity developed by authors in order to stimulate effective learning, Ophthalmology residents from the Faculty of Medicine, Thammasat

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University. The activity engages both residents and instructors in the learning and teaching process. All the photos were pre-selected and, during the challenge, guided to the correct answers and important details by qualified and experienced ophthalmology specialists.

Methods

Photo Challenge is a set of five ophthalmic photos and their related investigations creating by 7 ophthalmologists in 5 sub specialties. A list of common ophthalmic diseases is referred to American Academy of Ophthalmology textbook.(Table 1)

In this study, fifteen residents from three years of training were tested by pre and post Objective Structured Clinical Examination (OSCE) for objective evaluation. For subjective evaluation, a pre-post questionnaire was used.(Table 2)

All residents were randomized and divided into five groups to compete in a quiz and discuss the disease depicted. There will be only one photo for each group. The 1st year trainee will start first, then second and third year residents will have to add up what has not been previously described or discussed respectively. Later, qualified ophthalmologist instructors will score the team's performance on quality and completion of discussion and provide feedback on the conformity, rationale and omissions of the discussion as a team. This Photo Challenge was performed twice a month for 3 months. All residents attend all Photo Challenge activities. Then, all attendees were both subjectively and objectively tested after the activity finished. (Figure 1) Photo Challenge activity uses open question and let the competitors freely "describe everything you know" and discuss different aspects of the disease depicted in the photo as following topics : History taking, Physical examination, Investigation, Differential

Table 1: A list of common ophthalmic diseases in all Photo Challenge set

List of ophthalmic diseases in Photo Challenge activity	
Neovascular glaucoma	Vitreomacular traction
Trabeculoplasty	Fush heterochomic uveitis
Peters' anomaly	Glaucomatocyclitic crisis
Vogt-Koyanagi-Harada Disease	Thyroid eye disease
slow progressive myopia	Endophthalmitis
Krukenberg spindle	blepharophimosis syndrome
Aniridia	Nocardia keratitis
Pseudoexfoliation syndrome	Band keratopathy
Vortex keratopathy	Adrenochrome deposits
Keratoconus	Meesmann corneal dystrophy
Coloboma	Pseudoesotropia
Mobius syndrome	Orbital cellulitis
Epiblepharon	Epicanthus
Pilomatricoma	Congenital nevocellular nevus
Trichotillomania	Diabetic macular edema

Table 2 : Pre-questionnaire for subjective evaluation.

Pre-questionnaire: Circle appropriate level of your knowledge about the following topics															
	Glaucoma			Cornea			Retina			Pediatrics			Oculoplastic		
History taking	L	M	H	L	M	H	L	M	H	L	M	H	L	M	H
Physical examination	L	M	H	L	M	H	L	M	H	L	M	H	L	M	H
Investigation	L	M	H	L	M	H	L	M	H	L	M	H	L	M	H
Differential Diagnosis	L	M	H	L	M	H	L	M	H	L	M	H	L	M	H
Treatment	L	M	H	L	M	H	L	M	H	L	M	H	L	M	H
Prognosis	L	M	H	L	M	H	L	M	H	L	M	H	L	M	H

*L = low, M = moderate, H = high

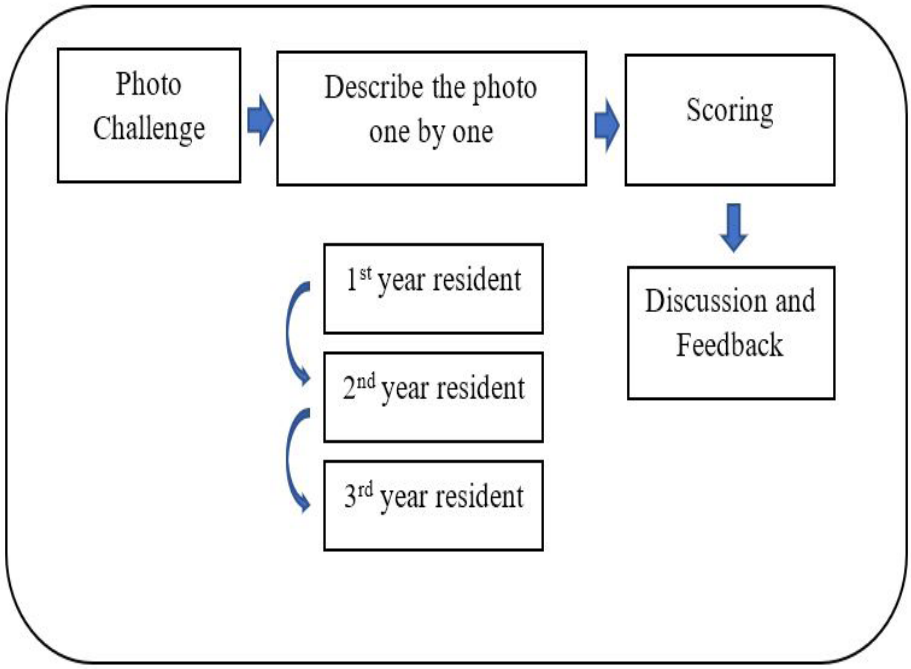

Figure 1: Study design

Diagnosis, Treatment and Prognosis.

Result

Subjectively, for all topics of knowledge in glaucoma, cornea and retina, all attendees provided improvement in knowledge level from moderate to high level. 80% of attendees gave high level of knowledge after attend all Photo Challenge activities in pediatrics and oculoplastic. A result of Objective assessment using pre and post Objective Structured Clinical Examination (OSCE) was shown in Table 3.

The mean assessment of post objective assessment using pre and post Objective Structured Clinical Examination (OSCE) shown statistically significant from 5.87 up to 8.00 out of 10. Also, all subjects give positive feedback about this innovative Photo Challenge. They favored the activity and benefited from engaging in the learning experiences as well as being given opportunities to practice clinical thinking processes by verbally approaching the clinical diagnosis from important findings and management of the disease.

The qualified instructors also provided positive feedback. They were able to perceived significantly improvement in last two Photo Challenged activity from all subjects. Clinical thinking process of all attendees was trended and well formed. The skills of history taking and clinical examination including investigation were properly performed. The knowledge of updated treatment was instructed by specialized ophthalmologists.

Discussion

Ophthalmology requires numerous image recognition. Apart from history taking, the clinical findings crucially assist clinical diagnosis. Thus, learning through images in Photo Challenge adjunct to the preceding teaching basis benefits students in several ways. It requires active learning method which forges deeper understanding through critical thinking. Also, it shifts the focus from passively digested information to energetically engagement with the activity. Moreover, it enhances a clearer understanding and aid students generate long-standing visual memories with the help of instructors.

The performance and clinical skills, including history taking, physical examination, investigation, differential diagnosis, treatment and prognosis of the disease, were significantly improved among subjects by observation and feedback. This educational course also changes in the learning behavior of the students who showed continuous enthusiasm for learning.[5]

While, traditional clinical teaching such as lecture, case report and OPD observation, are altogether using passive learning method. There are several disadvantages, which are time limitation when providing outpatient services, inadequate teaching materials, lack of teaching plan in advance, problems with noncooperative patients and its shorter span memory formed to students, compare to the photo challenge activity.

Conclusion

Photo-Challenge activities, unlike the traditional photo quiz, are engaging for learners and enable them to demonstrate knowledge and skill in clinical thinking,

Table 3 : A result of Objective assessment using pre and post Objective

	Mean score before class	Mean score after class	Improvement score**
OSCE*	5.87+-1.13	8.00+-1.25	2.13+-083

*OSCE = Objective Structured Clinical Examination
**All *P* were < 0.001 for the change in OSCE scores

applicable to everyday practice and, in addition, evaluate themselves after the quiz. Instructors are able to emphasize knowledge and guide clinical thinking relevant to the learning outcomes after each session. It can be noted that the Photo Challenge is evidently more suitable for producing intended results than traditional photo quiz in Ophthalmology studies. The Photo-Challenge's success demonstrates a counterpart of a teaching method that emphases visual detection of clinical signs and clinical thinking as learning outcomes, in context of Ophthalmology learning.

Limitations

Our study is a supplementary teaching method whereas our subjects still attended traditional teaching methods at that period. Therefore, we included every available resident regardless of their different basic knowledge and performance and style of learning, which the results may vary upon individual. The sample size is also relatively small. Finally, we did not follow the subjects' long-term retention of knowledge.

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