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January-June 2019

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Editor's Letter

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



To our readers,

I would like to welcome you to EyeSEA journal. Our continued growth of authorship and readership has been reflected in the great variety of articles compiled in this current release. This success is made possible thanks to our many authors, reviewers, editors from a growing network of contributors.

We continue our focus on publishing data that represents the South East Asian population in all domains of Ophthalmology ranging from normative values of pediatric retina to the changes of the cornea after common procedures such as excimer laser refractive surgery and pterygium excision. Furthermore, we present you a thought-provoking collection of case reports from across all subspecialties throughout the South East Asian region.

Our editorial team is committed to the constant improvement of publication standards, supported by your great contributions of literature. We are driven to attain the highest level of international recognition and readership.

Warmest regards,

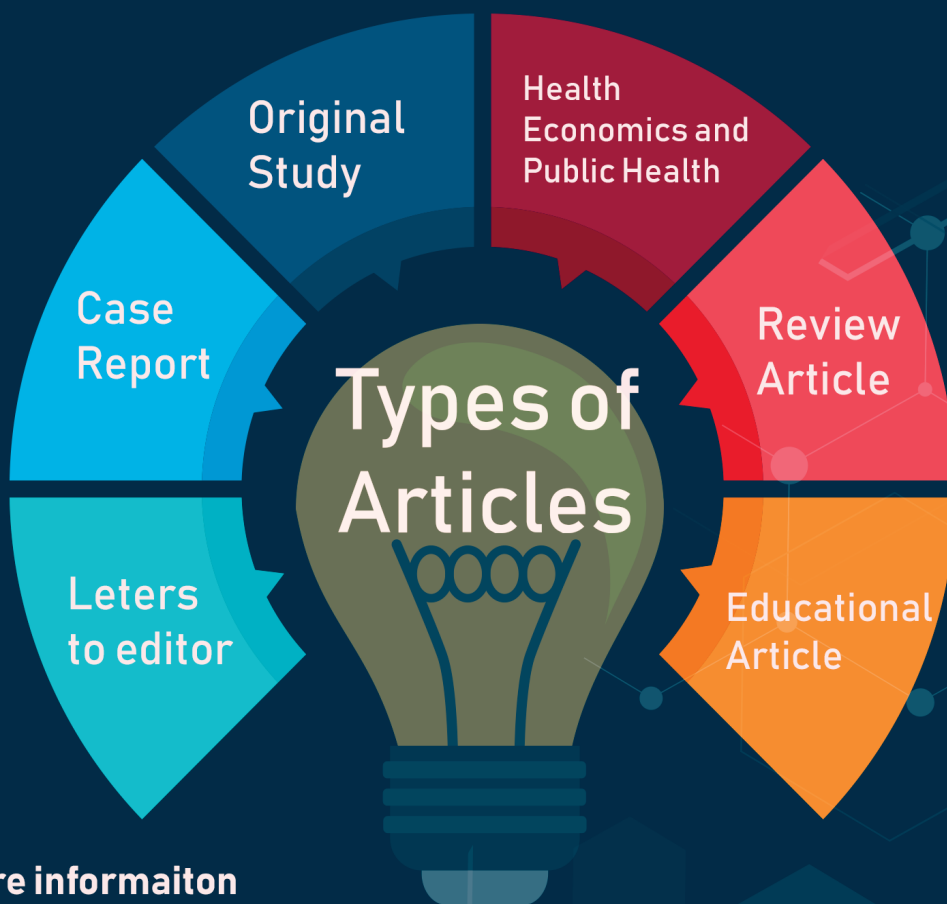
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Aims and Scope and Publication Policy

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.

Publication Policy

Dates and Distribution

Publication frequency is twice per year (once every 6 months)

Issue 1 : January - June , Author Submission Deadline: 31st of March

Issue 2 : July - December , Author Submission Deadline: 30th of September

Each issue will contain a minimum of 5 articles, up to a maximum of 12 articles

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Key Words: minimum 2, maximum 5

Your abstract must contain content for the following headings:

- 1.Title
- 2.Purpose ("Background" for case report)
- 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
- 6.Conflicts of Interest
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Background

- This section should be the shortest part of the abstract and should very briefly outline the following information:
- What is already known about the subject, related to the paper in question
- What is not known about the subject and hence what the study intended to examine (or what the paper seeks to present)

Methods

- What was the research design? e.g. Diagnostic Study, Etiognostic Study, Prognostic Study, Therapeutic / Efficacy Study -in addition to the study method: Case report, Case Control, Cohort, Randomised Controlled Trial.
- What type of patients are recruited?
- What was the clinical setting of the study? (if relevant)
- How were the patients sampled
- What was the sample size of the patients? (whole/and or in different groups)
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-What was the primary outcome measure and how was it defined?

Results

- The number of patients who completed the study; dropout rates in the different groups and their causes
- The results of the analysis of the primary objectives, mentioning statistical method, expressed in words and numbers along with P values in parenthesis
- The results of the analysis of the more important secondary objectives
- Numerical information about the above analysis such as in terms of means and standard deviations, response and remission rates. Wherever possible: effect sizes, relative risks, numbers needed to treat, and similar statistics should be provided along with confidence intervals for each.
- Important negative findings, if any should also be presented: that is, findings that fail to support the authors' hypothesis
- Data on important adverse events should be included in addition to the data on efficacy

Conclusion

- The primary take-home message
- The additional findings of importance
- The perspective

Our guidelines are based on the following reference:

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Abbreviations

Abbreviations should be defined at the first mention in the text and also in each table and figure. For a list of standard abbreviations, please consult the Council of Science Editor Style Guide or other standard sources. Write out the full term for each abbreviation at the first use unless it is a standard unit of measure.

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Manuscripts should be organized under the following four main headings:

- Introduction
- Methods
- Results
- Discussion
- Conclusion
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- To aid EyeSEA formatting editors in publishing your article in a uniform format in both printed and electronic versions, we recommend you write your paper in the following format:

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Bilateral idiopathic frosted branch angiitis in an older patient

Han Nie Han Chng¹, Fazliana Ismail², Kiet Phang Ling²

¹University of Malaya Medical Centre,

²Hospital Sultanah Bahiyah

Background: To report the oldest age to our best knowledge presentation of idiopathic frosted branch angiitis (FBA) in the Asian population and its characteristics.

Methods: Case Report

Results: This is a rare case of bilateral fulminant frosted branch angiitis at older age of presentation and prolonged course of visual recovery with poor visual outcome in one eye. 58-year-old Malaysian female patient, presented with sequential involvement of both eye, initially right eye panuveitis, frosted branch angiitis and subretinal fluid at macula area then the left eye. Bilateral vision was hand movement. The laboratory investigation including autoimmune disease, infectious disease and vitreous sample for viral and tuberculosis PCR were negative. Patient was treated with systemic steroid for a total duration of 6 months. Intravenous Acyclovir was initiated followed by oral Acyclovir. Vitritis reduced, exudative retinal detachment and vasculitis resolved but vision remained poor. Her vision slowly regained after 3 months of treatment and at 6 months her best corrected visual acuity for right eye was 2/60 due to ischemic maculopathy and left eye was 6/9.

Conclusion: Older age groups may present with more severe anterior and posterior inflammation compared to a younger age group, therefore prolonged and timely corticosteroid treatment is crucial for good visual outcome.

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

Keywords: idiopathic, frosted branch angitis, bilateral

EyeSEA 2019;14(1): 1-4

Full text. <https://www.tci-thaijo.org/index.php/eyesea/index>

Background

Frosted branch angiitis (FBA) is a severe form of vasculitis with characteristic fundus appearance of 'frosted branches of a tree' due to the infiltration of perivascular space with inflammatory infiltrates.

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Despite the severe retinal appearance, the prognosis is usually good, with rapid recovering of visual acuity after steroid treatment.

Case history

58-year-old Malaysian female patient with no known medical illness presented to our eye clinic with right eye sudden blurring of vision for 2 days duration. It was associated with mild eye redness and

discomfort. She gave a history of low grade fever 3 days prior to the blurring of vision. Visual acuity of the right eye and left eye was hand movement and 6/9 respectively. Relative afferent pupillary defect was positive in the right eye. Anterior segment examination revealed anterior chamber cells of 4+ with posterior synechiae and presence of anterior vitreous cells in the right eye. Posterior segment examination showed vitritis, dense perivascular exudates and frosted branches appearance at the periphery (Figure 1).

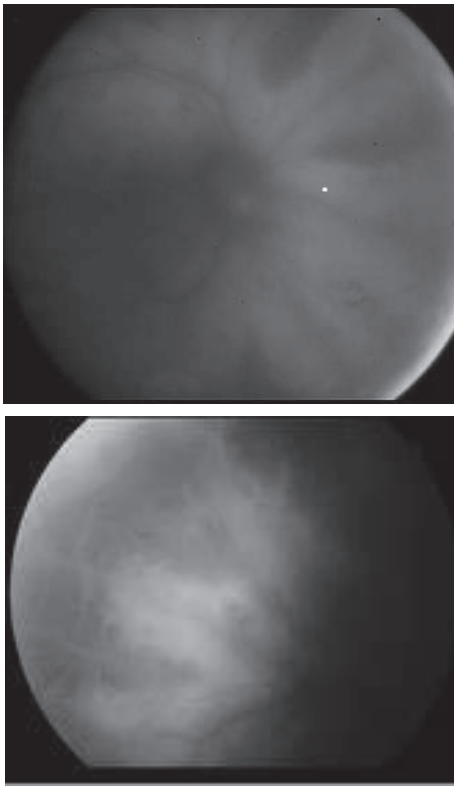


Figure 1: Fundus photos of the right eye

There were scattered small retinal haemorrhages in all 4 quadrants and subretinal fluid at the macula area. Anterior and posterior segment examinations of the left eye were normal (Figure 1). However two days later patient complained of sudden

blurring of vision on the left eye with visual acuity dropped to hand movement. Anterior segment examination showed anterior chamber cells of 2+. While posterior segment examination revealed mild vitritis, scattered small retinal haemorrhages, diffuse vascular sheathing with frosted branches appearance at the periphery and subretinal fluid at the macula area. Fundus fluorescein angiography on both eyes showed diffuse leakage from the vessels and discs (Figure 2,3) at late phase with no evidence of vascular occlusion.

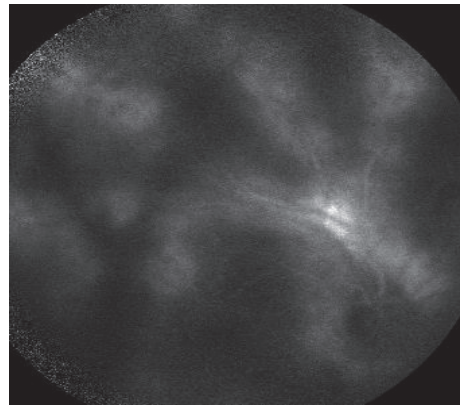


Figure 2: FFA of the right eye showing diffuse vascular leakage at late phase

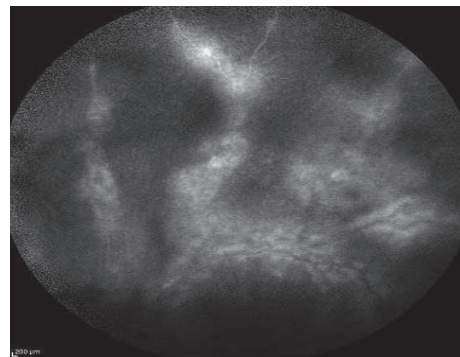


Figure 3: FFA of the left eye showing diffuse vascular leakage at late phase

Vitreous sample was sent for cytomegalovirus, herpes simplex virus, varicella zoster virus and Mycobacterium

tuberculosis polymerase chain reactions (PCR). Blood investigations including autoimmune and infectious disease screening were sent. All PCR results and blood investigations were negative. Masquerade condition was also ruled out with negative findings on systemic examination as well as the tumour markers on blood investigations. Based on the clinical presentations and negative investigations for secondary causes, the diagnosis of bilateral idiopathic FBA was made. It was possibly triggered by viral antigen in view of history of low grade fever prior to presentation. Intravenous methylprednisolone was then initiated promptly, 1 g/day for 3 days and then continued with high dose oral prednisolone 1 mg/kg/day with subsequent tapering dose for 6 months. She was also started on intravenous acyclovir 750 mg three times a day for 2 weeks and completed 6 weeks course of oral acyclovir. With treatment, bilateral eye vitritis, subretinal fluid at macula area and vasculitis resolved. However, both eyes vision remained as hand movement. After 3 months, her left eye vision gradually improved with best corrected visual acuity of 6/9 at 6 month. Unfortunately the right eye best visual acuity at 6 month was only 2/60 due to ischaemic maculopathy.

Discussion

Idiopathic FBA predominantly affects the young and healthy patient with female preponderance. It has a bimodal age distribution with one peak in childhood and a second in the third decade. Walker et al¹ reported that, the age of presentation range from 2 to 42 years old. In 2012, the youngest case of FBA at the age of 11 months old had been reported.² While the oldest patient reported with FBA was 80 years old from Australia and was associated with infective endocarditis.³ Another 2 cases reported from Japan with age presentation

of 62 and 69 years old. Both were associated with aseptic meningitis and acute chorioretinal insufficiency respectively.^{4,5} From the literature review, our patient is the oldest reported case of idiopathic FBA without other ocular or systemic association. In idiopathic FBA, the cause is unknown but suspected to be viral.⁶ However the onset of FBA after prodromal illness in 33% of the cases suggest possible hypersensitivity reaction to various infective agents with immune complex deposition.¹ Secondary causes of retinal vasculitis such as multiple sclerosis, acute retinal necrosis, cytomegalovirus, herpes zoster, herpes simplex, HIV and adenovirus infections, pars planitis, Eales disease, syphilis, tuberculosis, and sarcoidosis should be ruled out.⁷ In older age group, we need to consider masquerade signs secondary to intraocular lymphoma or leukemia with retinal infiltration.⁸ Other than the characteristic fundus of frosted branches of a tree, intraretinal edema, intraretinal hemorrhages, papillitis, vitritis, and iritis can be present. Veins are more affected than arteries. Older patients tend to present with severe anterior and posterior inflammation compare to younger age group.^{3,4,5} FFA will demonstrate normal venous flow and delayed filling of arteries in the early phase, then leakage from vessels (veins more than arteries) in the late phase without vascular occlusion or stasis.¹¹ Visual field test may reveal constriction of visual field or central scotoma secondary to macular edema. Electroretinogram, electrooculogram and visual evoked potential may show reduced amplitudes due to reduced function of the retina and optic nerve.¹ FBA usually responds well to systemic corticosteroid therapy with good and rapid visual recovery.^{1,7} Intravitreal and posterior subtenon injection of triamcinolone had been described with success.^{2,11} Due to postulated possible viral etiology, acyclovir has been used with unknown effect.¹ In

the more recent report, Adalimumab had been used with good response.⁹ Walker et al¹ reported 3 cases without treatment, yet have an excellent visual outcome. In another recent case report, a pregnant woman with bilateral idiopathic FBA had spontaneous clinical improvement without treatment and fully resolved postpartum.¹⁰ However in our case, timely treatment with corticosteroid therapy resulted in good vision in the left eye. Unfortunately for the right eye, there was a delay in treatment for few days which led to poor visual outcome secondary to macular ischemia. Apart from that, our patient had longer recovery of visual acuity despite corticosteroid treatment. This is similar to the two reported cases in Japan.^{4,5}

Conclusion

In conclusion, we are reporting the oldest age presentation of idiopathic FBA. In the older age group, they can present with severe panuveitis and require a longer recovery period unlike the younger age patients. Hence, a prolonged course of corticosteroid treatment is needed. With the possibility of complication such as macular ischaemia, immediate administration of corticosteroid therapy is advocated. In such cases may consider anti-tumour necrosis factor such Adalimumab which had been reported to have rapid and long lasting effect on visual improvement however more studies needed to support its use in idiopathic FBA.⁹

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A rare case of complex orbital lymphangiohemangioma

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Background: Complex orbital lymphangiohemangioma is a rare benign vascular lesions. It usually appears as an enlarging mass without specific clinical features and frequently misdiagnosed. This case report highlighted a case of orbital vascular anomalies which presented as intramuscular hemangioma with lymphangioma.

Results: A 12 years old boy with underlying bronchial asthma, presented with painless progressive enlarging swelling over right medial canthal area and right upper lid since age of 6 years old. His best corrected vision was OD 20/50, OS 20/20. Right eye showed non tender mass at medial canthal area with no skin changes. Anterior chamber and posterior chamber bilateral eye was unremarkable. CT scan showed soft tissue swelling at the medial part of the right orbit involving the medial part of upper and lower eyelid and medial canthal region, measures approximately 2.1cm x 2.4cm x 3.9cm with blocked nasolacrimal duct suggestive of mucocele. Excision biopsy was performed, the intraoperative findings revealed a mass mixed with fibrosis tissue and microcyst with no definite plane with underlying skin and orbicularis oculi muscle. Histopathology examination showed benign vascular lesion likely intramuscular angioma. 3 weeks post operatively, he developed wound breakdown and exploration under GA was done, which intraoperatively showed multiple small slow oozing from remnant of the lesion with multiple cyst surrounding wall of cavity, bluish lesion and small telangiectatic vessels were seen at the upper lid.

Conclusion: Complex orbital lymphangiohemangioma is a rare benign vascular lesion. The recurrence rate is high even after wide surgical excision due to its microscopically infiltrative pattern of diffusion into the surrounding muscular tissue. Long term clinical and radiological follow up are strongly recommended in order to precisely diagnose and treat further recurrences.

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

Keywords: benign vascular lesion, hemangioma, intramuscular hemangioma, lymphangioma, lymphangiohemangioma.

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Background

Vascular anomalies differentiated into two groups based on endothelial characteristics: hemangiomas and vascular malformations, by Mulliken and Glowacki classifi-

cation 1982. Depending on the type of vessel involved, vascular malformation group was subdivided into high-flow (such as arteriovenous malformation and arteriovenous fistula) and low-flow (such as venous and lymphatic malformation). Intramuscular angioma is a rare special form of hemangioma. It is benign form of tumor in which less than 1% of hemangiomas in the body occur in skeletal muscles, and less than 20% of these occur in the head and neck region arising most frequently in the masseter and trapezius muscle.¹ In contrast to the cutaneous hemangiomas of infancy, it never regresses spontaneously.² It usually appears as an enlarging mass without specific clinical features and is therefore frequently misdiagnosed.³ The distinction between lymphangiohemangioma and intramuscular hemangioma is not clear and has been used interchangeably given the overlapping clinical, histologic and imaging features. The recurrent rate following surgical excision in orbital lymphangioma are 52% as reported by Char et al¹³, 11% by Gündüz et al¹⁴, while in IMH were reported to be 20% in capillary type, 9% in the cavernous type and 28% in mixed type IMH.¹ This is the reported case of orbital vascular anomalies which presented as intramuscular hemangioma with lymphangioma. To the best of our knowledge, the coexistence of both of hemangioma and lymphangioma is unusual and has been reported only in few cases.

Case history

In 2017, a 12 year old boy with underlying bronchial asthma, was referred for the further management of right orbital tumor which presented with painless progressive, no compressible swelling over right medial canthal area and right upper eyelid since age of 6 years old. Otherwise no history of pus discharge from the swelling, no changing of size during Valsalva maneuver and he has no history of eye trauma. There is no

history of malignancy or blindness in his family. On examination, his best-corrected visual acuity was 20/50 OD and 20/20 OS. Right eye showed nontender mass at medial canthal area with no overlying skin changes (figure 1) with subconjunctival multiple cystic lesions medially (figure 2). Otherwise anterior segment and posterior segment bilateral eye was unremarkable.



Figure 1: Right medial canthal mass.

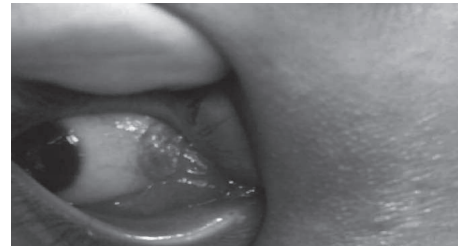


Figure 2: Right eye subconjunctival cystic lesion

Computed tomography (CT) showed soft tissue swelling at medial part of right orbit involving medial part of upper and lower eyelid and medial canthal region, measuring 2.1cm x 2.4cm x 3.9cm with increase density of lateral part of lesion. Right globe and medial rectus muscle are pushed laterally. Streakiness of extraconal fat and slight flattening of nasal bridge with blocked nasolacrimal duct. (figure 3) Right excision biopsy of right medial canthal mass and conjunctival lesion was done. Intraoperatively the tumor size was 2.5cm (width) x 1.0cm (height) and it was mixed with fibrosis tissue and microcyst (specimen A) (figure 4 and 5). It has no definite plane with overlying skin and orbicularis muscle. Multiple cyst of right conjunctival lesion

(specimen B). Nasolacrimal duct was patent. Specimen A and B were given for histopathology examination.



Figure 3: CT findings showed soft tissue swelling at medial part of right orbit involving medial part of upper and lower eyelid and medial canthal region.

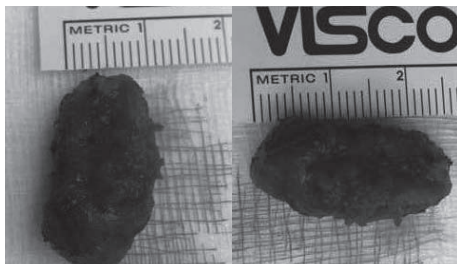


Figure 4 and 5: Macroscopic specimen of the lesion.

Macroscopic examination

A: Specimen consists of a piece of brownish tissue fragments measuring 25x10x10mm. Cut section shows homogenous greyish fragment with areas of hemorrhage. Bisected and submitted entirely in 2 blocks.

B: Specimen consists of 3 fragments of brownish to greyish tissue fragments measuring 2x2x2mm, 4x2x1mm and 5x2x1mm.

Microscopical examination:

A: Sections show fragment of fibrocolla-

geneous tissue interspersed with adipose tissue and skeletal muscles. There are various sized vascular channels present with focal thrombosis. No evidence of malignancy seen. (figure 6)

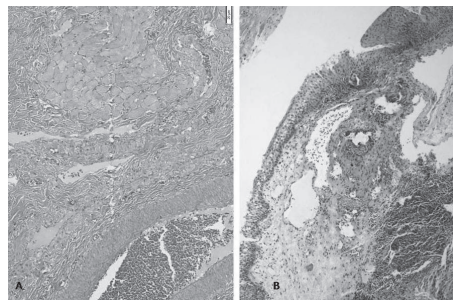


Figure 6: A: Fibrocollagenous tissue interspersed with adipose tissue and skeletal muscles with various sized vascular channels present.

B: Tissue lined by conjunctival epithelium with underlying stroma shows presence of dilated lymphatic spaces and consist of patchy lymphocytic infiltrates is seen between the dilated spaces.

B: Levels show fragments of tissue lined by conjunctival epithelium consists of several layers of columnar cells that contain mucin secreting goblet cells. The underlying stroma shows presence of dilated lymphatic spaces lined by flattened epithelium. Patchy lymphocytic infiltrate is seen in between the dilated spaces. No malignancy seen.

Specimen A was consistent with benign vascular lesion, intramuscular angioma and specimen B was consistent with conjunctival lymphangioma.

Three weeks following the operation, the patient developed wound break down over right medial canthal wound due to the collection of blood underneath the wound (figure 7). Wound exploration and resuturing was done. Intraoperative noted multiple small slow-oozing bleeding from remnant of the lesion with multiple small cystic lesion surrounding of the wall of cavity. A bluish lesion and small telangi-

ectatic vessels at the upper eyelid noted. Postoperatively, there were some residual of the lesions (figure 8).



Figure 7:Wound breakdown



Figure 8:After resuturing with minimal residual

During 1 month post operative follow up, MRA and sclerosing therapy was offered to patient and he was further his follow up at different hospital for sclerosing therapy.

Discussion

Intramuscular angioma is the rare special form of hemangioma. It is benign form of tumor in which less than 1% of hemangiomas in the body occur in skeletal muscles, and less than 20% of these occur in the head and neck region arising most frequently in the masseter and trapezius muscle.¹ In contrast to the cavernous hemangiomas of infancy, it never regresses spontaneously.² It usually appear as an enlarging mass without specific clinical features and is therefore frequently misdiagnosed.³

In the histological classification, intramuscular hemangiomas are subdivided according to their vessel size; capillary, cavernous and mixed form, Beham et al showed in their work that many cases the mixed form prevails⁴ as in our case, lesion showed fragment of fibrocollagenous tissue interspersed with adipose tissue and skeletal

muscles with various sized vascular channels present with focal thrombosis.

Intramuscular hemangioma often remains undiagnosed preoperatively⁵ but its nature may be suggested by MRI, where the tumor will often appear as sharply demarcated, images. This is due to stagnant blood in the larger vessels.⁶ Linear areas, isointense to fat and muscle, are often observed in the lesions representing fibro-fatty septae between vessels. Usually radiological distinction between different types of IMH is not possible.^{6,7} Intramuscular hemangioma is poorly defined by CT.⁷

Orbital venous lymphatic malformations, previously known as lymphangiomas, are uncommon and sometimes referred to as no-flow or low-flow vascular malformations. They contain abortive vessels, which spread among normal structures and present as an unencapsulated, primarily thin-walled masses with numerous cystic spaces of different size. They show tendency to spontaneous haemorrhage, resulting in a sudden onset of proptosis combined with periorbital swelling and reduced eye motility, at times leading to optic nerve compression.⁸ On imaging they present as an infiltrative, multilobulated mass with poor encapsulated, also intra and extraconal, sometimes harboring calcifications seen on CT. MR imaging is the modality of choice for the evaluation of lymphatic malformations because it best depicts at various components. T1-weighted images best depict lymphatic and proteinaceous fluid, and T1-weighted fat-suppressed images are best for detecting blood or blood products. T2-weighted fat-suppressed images provide improved visibility of component that contain non-hemorrhagic fluid.⁹ Fluid-fluid levels produced by hemorrhages of various ages within multiple cysts are almost pathognomonic.¹⁰ In our case, histopathology of conjunctival lesion showed tissue lined by conjunctival epithelium with underlying stroma shows presence

of dilated lymphatic spaces and consist of patchy lymphocytic infiltrates was seen between the dilated spaces.

Treatment of both intramuscular hemangioma and lymphangioma are challenging. Because of the high rate of recurrence, the best treatment for intramuscular hemangioma is total surgical excision² as well as for lymphangioma. However the total surgical reception are difficult for lymphangioma. Recurrence rates of IMH were reported to be 20% in capillary type, 9% in the cavernous type and 28% in mixed type IMH.¹ As for the present case, patient developed wound breakdown due to collection of blood underneath the wound and due to incomplete excision of lesion.

A conservative therapy should target the abnormal membranes that make up the lymphangioma, while sparing the adjacent normal tissue through which the lymphangioma infiltrates. Sclerosing therapy has the potential to supply some of these benefits.¹¹ The idea of using sclerotherapy in the treatment of lymphangioma occurred when it was noted that lymphatic malformations spontaneously involute when they became infected and the infection resolved. Sclerosing agents may have specificity for the abnormal tissues if introduced intralesionally. The first case of lymphangioma treated by sclerotherapy was reported in 1933, using sodium morrhuate. Injection of sclerosing agents has proven efficacy in lymphangiomias in other locations. Some sclerosing agents have been tested in OL, such as sodium tetradecyl sulfate, sodium morrhuate, and OK 432, with different rates of success, although with limited numbers of patient and some local complications, such as pain, swelling, and haemorrhage.^{11,15,16} Complete tumour regression was noted in 6 weeks following intralesional injection.¹² There is insufficient evidence demonstrating its efficacy at present. As in our case, patient still has residual lesions after total exci-

sion, and he was opted for sclerotherapy.

Conclusion

Complex orbital lymphangiohemangioma is a rare benign vascular lesions. The recurrence rate is high even after wide surgical excision due to its microscopically infiltrative pattern of diffusion into the surrounding muscular tissue. Long term clinical and radiological follow ups are strongly recommended in order to precisely diagnose and treat further recurrences.

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Descemet membrane detachment post-viscoelastic injection for ocular hypotony

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Background: To report a case of extensive Descemet membrane detachment treated with repeated air Descemetopexies and venting incisions.

Results: A 69-year-old diabetic and hypertensive man with medically uncontrolled mixed POAG and pseudophakic glaucoma underwent left eye Ahmed valve implantation. Although the implantation was uneventful, the eye had a shallow anterior chamber (AC) with iridocorneal touch on the first post-operative day, due to overfiltration. We performed AC reformation using Healon GV on the same day. The following day, an extensive Descemet membrane detachment was seen, confirmed by anterior segment optical coherence tomography (AS-OCT). With non-resolution after 1 week, and worsening of vision to hand movement perception, we performed Descemetopexy and AC reformation with Healon GV on day 8 after the initial surgery. On day 16, visual acuity was 6/24 although there was still partial detachment of the Descemet membrane. We repeated Descemetopexy with venting incisions. The detachment completely resolved after 20 days. About 2 months later, visual acuity was 6/24 with mild interface scarring. IOP was well controlled.

Conclusion: Early and repeated Descemetopexy in extensive Descemet membrane detachment can lead to reattachment and return of useful vision.

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

Keywords: Ahmed Glaucoma Valve, Descemetopexy, Descemet Membrane detachment
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Background

Descemet Membrane Detachment (DMD), first reported in 1928 by Bernard Samuels¹, occurs when there is a separation of the endothelium-Descemet Membrane complex from the posterior corneal stroma. It is a potentially serious complication of intraocular surgery or trauma. It most often occurs after cataract surgery, but can also occur after

a wide range of ophthalmic procedures. The natural history of DMD has long been an area of controversy, and the appropriate timing for intervention remains unclear.² Most DMDs remain small and localized to the wound, but some cases can present with large, extensive detachments which result in severe corneal edema, a double anterior chamber, corneal decompensation and reduced visual acuity. Most surgeons attempt to reattach the membrane by injecting air, slowly-reabsorbing gases, or viscoelastic substances into the anterior chamber.¹ The literature also contains reports of spontaneous reattachment of large DMD.²

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Descemet Membrane detachment post glaucoma surgery and Ahmed Glaucoma Valve implantation is unusual.⁴ Its management is more challenging since the eye is no longer a closed system and tamponade agents can escape through the tube.⁴ We present a case of Descemet Membrane Detachment (DMD) in a patient who underwent uneventful Ahmed Glaucoma Valve (AGV) implantation but was complicated by early post-operative shallow anterior chamber (AC) and hypotony. Viscoelastic (Healon GV) was injected into the AC on the 5th post-op day but this was complicated by a large central DMD, confirmed by anterior segment optical coherence tomography (AS-OCT). Surgical intervention led to Descemet Membrane reattachment and satisfactory visual outcome.

Case history

A 69-year-old diabetic Chinese man with medically uncontrolled, mixed POAG and pseudophakic glaucoma underwent left eye Ahmed Glaucoma Valve (AGV) implantation. About 5 years before that, he had a complicated left eye cataract operation done at another centre. At that time, the patient had intraoperative iris prolapse and iris trauma. Subsequently, he had slow visual recovery, with prolonged anterior chamber inflammation. He also developed secondary glaucoma post operatively, with intraocular pressures (IOP) ranging from 20-30 mmHg with maximal medical treatment. In September 2016, the patient underwent left eye micropulse laser trabeculoplasty. The IOP came down for few months but later increased again. Just prior to the AGV surgery, the patient's best corrected visual acuity (BCVA) for both eyes was 20/25. IOP was 20 mmHg in the right eye with one antiglaucoma medication, and 30 mmHg in the left eye with 4 antiglaucoma medications. On examination, both eyes had clear corneas and deep anterior chambers. Fundus exam-

ination showed cup:disc ratios (CDR) of 0.8 in both eyes. The macula and peripheral retina were normal. On gonioscopy, the right eye angle was open but the left eye had peripheral anterior synechiae in the superior and inferior quadrants. Although the AGV implantation was uneventful, on the 1st post-operative day, the patient had a shallow anterior chamber (AC) with iridocorneal touch due to overfiltration. The IOP was 5 mmHg. The patient underwent AC reformation with Healon GV on day 2 and day 5 post operatively, at the slit lamp microscope from the side port at 2 o'clock. During the second AC reformation, part of the Healon GV entered the space between the Descemet Membrane and posterior corneal stroma, causing a large central Descemet Membrane detachment. His visual acuity dropped to hand movement due to significant corneal edema. The detachment was confirmed with anterior segment optical coherence tomography (AS-OCT) (Figure 1).

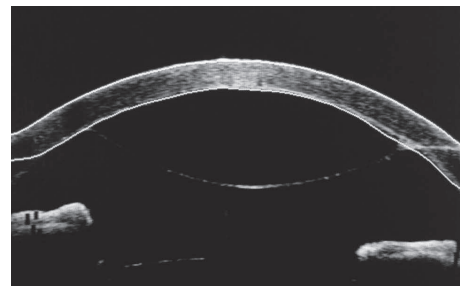


Figure 1: AS-OCT showed central Descemet Membrane Detachment post AC reformation with Healon GV

He underwent surgical intervention for DMD. Intraoperatively, an attempt was made to release the viscoelastic from the side port at 2 o'clock by gently pressing on the posterior lip of the wound while a new side port was made at 4 o'clock to inject Healon GV into the anterior chamber.

The first Descemetopexy was attempted with a cohesive viscoelastic as air or gas would have easily escaped through the AGV tube. No venting incision was attempted as escape of cohesive viscoelastic through the small incisions was assumed not possible. Post-operatively, a bandage contact lens (BCL) was applied and the patient was treated with Gutt Pred Forte and Gutt Vigamox 2 hourly. Post-intervention, there was still a persistent partial Descemet Membrane Detachment, for which the patient underwent a second procedure one week later. The reason to wait for 1 week was to let the viscoelastic degenerate so it would become easier to express out of the trapped space. During the second surgical procedure, again the initial side port was depressed to release the remaining viscoelastic trapped in the space and it was noted to have liquified. Subsequently, non-expansile 12% C_3F_8 was injected into the anterior chamber and 4 venting incisions were made. Venting incisions were made at the second surgery as we expected the viscoelastic to have liquified so it would be easier for it to escape through the incisions. Post-operatively, another BCL was applied and the patient given G. Pred Forte and G. Vigamox 2 hourly. The patient responded well to this intervention, and the cornea became clear and detachment resolved completely. At his last follow up, the patient's refraction was $+0.25/-1.00 \times 55$ (6/6⁻²) for his right eye and $+2.00/-1.00 \times 45$ (6/30 ph 6/24) for his left eye. Endothelial cell count was done, which was 4427 cells/mm² for his right eye and 1172 cells/mm² for his left eye. The cornea had mild interface scarring but AS-OCT showed no more Descemet Membrane detachment (Figure 2). The IOP was also well controlled at 16mmHg. Currently 2 years post operatively, his vision remain good and IOP well controlled with 2 anti glaucomas

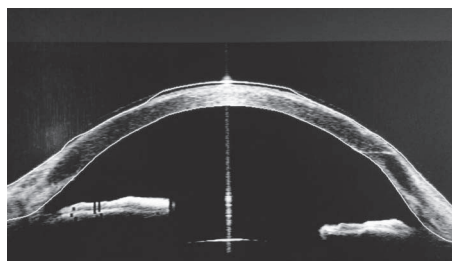


Figure 2: AS-OCT of resolved Descemet Membrane Detachment after venting incision.

Discussion

Descemet Membrane Detachment (DMD) is a rare but sight-threatening complication. Predisposing factors include shallow AC, accidental insertion of instruments or saline or OVD between the posterior stroma and DM, blunt keratomes, or weak adhesions between the posterior stroma and DM.³⁻⁶ In our case, accidental injection of Healon GV between the posterior stroma and DM was the cause of DMD. Sometimes diagnosis of DMD on slit lamp examination may be difficult due to significant corneal edema.⁴ AS-OCT is thus a useful tool to diagnose and monitor the progress of DMD.⁷

Minor DMD may resolve spontaneously without medical intervention, but large detachments should be repaired in a timely manner as there is potential for irreversible damage to the cornea.⁴ The management includes both medical and surgical treatments, depending on the size and severity of the detachments.^{2,4}

In our case, one of the lessons to be learned is that viscoelastic (or other liquids e.g. balanced saline) injection, especially into shallow anterior chambers, should be performed with the use of microscopes. This would enable easier visualisation of the tip of the cannula, to ensure proper placement inside the anterior chamber before injecting. In reforming anterior chambers, a common viscoelastic used is Healon GV as its properties are very suitable in an-

terior chamber reformation post filtration surgery. It has high molecular weight and high viscosity up to 500,000 times that of aqueous humour.⁹ The molecules are easily deformed and it has been reported that Healon GV remains in the anterior chamber for less than 6 days.⁸ It was explained in our case that the first intervention was to release the viscoelastic through the side port. Only after 1 week when we expected the Healon GV to have degraded, then we do the venting incisions, and indeed it was easily expressed from the trapped space.

Conclusion

Descemet Membrane Detachment (DMD) after injection of viscoelastic into the anterior chamber is a known complication and can lead to severe and extensive corneal edema. Early recognition and repair of the detachment may prevent complications, such as corneal decompensation, corneal opacities and oedema, and an overall decline in visual acuity.

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A rare case of ocular toxoplasmosis complicated by both retinal detachment and choroidal neovascularization in an immunocompetent patient

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Background: To report an unusual case of ocular toxoplasmosis complicated by both retinal detachment and choroidal neovascularization in the same eye of an immunocompetent patient

Results: A 74-year-old gentleman of oriental origin presented with a 3-month history of reduced vision in the left eye: best corrected visual acuity was 6/6 in the right eye and 6/24 in the left eye. Clinical examination revealed no signs of systemic illness. The anterior segment in the left eye showed pigmented granulomatous keratic precipitates. Anterior chamber was deep with 3+ cells; no hypopyon. Both eyes were pseudophakic with clear media. Posterior segment of the left eye showed dense vitritis, with 2 areas of retinitis. No retinal breaks were visible. Serum Toxoplasmosis antibodies IgM was negative, but IgG was positive at 3.584. Vitreous tap was negative for CMV, HSV1, HSV2, and VZV DNA. Vitreous PCR for toxoplasmosis was not available at the time. He was started on oral Prednisolone 1 mg/kg, oral Bactrim (Sulfamethoxazole and Trimethoprim), and topical prednisolone acetate 1% (PredForte) 4-hourly. Visual acuity in the affected eye was 6/9 at 8 weeks post initiation of treatment. He subsequently developed retinal detachment which was operated with a visual outcome of 6/18. Unfortunately, he then developed choroidal neovascularization, and despite anti-VEGF treatment, did not regain his vision.

Conclusion: Prompt diagnosis of atypical presentation of ocular toxoplasmosis may aid management and subsequent preservation of visual function.

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

Keywords: Toxoplasmosis, Retinal detachment, Choroidal Neovascularization

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Background

Toxoplasma gondii is an obligate intracellular protozoa capable of infecting humans and other mammals. It has a worldwide distribution and is known to infect up to one third of the

world's population.¹ The etiological spectrum of infectious uveitis differs throughout the world because of various factors including geographic and demographic factors.² This case describes a case of presumed ocular toxoplasmosis complicated by retinal detachment and choroidal neovascularization.

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Case history

A 74-year-old gentleman of oriental ori-

gin with underlying hypertension, benign prostatic hyperplasia, and a non-functioning pituitary adenoma, presented with a 3 month history of reduced vision in the left eye. He was initially treated with Predforte and Azarga prior to presenting at our centre for a second opinion.

Both eyes were pseudophakic, performed at a private center, without any known complications. He denies any history of prodromal flu-like illness, tinnitus, chronic cough, night sweats, or fevers. He also denies any ulcers or joint pains. There was no history of penetrating eye injury. He lives at home with his wife and 3 children, all of whom are healthy. They do not have any pets at home. He retired from being a consultant designer at age 60. He gave a history of recent travel to Philippines a month prior to presentation. He is an ex-smoker and his regular medications were Losartan 50 mg OD, Amlodipine 10 mg OD, and Simvastatin 10 mg ON.

Clinical examination revealed no signs of systemic illness. There were no skin changes such as rashes or alopecia. At presentation, best corrected visual acuity was 6/6 in the right eye and 6/24 in the left eye. The anterior segment in the left eye showed pigmented granulomatous keratic precipitates (Figure 1). Anterior chamber was deep with 3+ cells; no flare or hypopyon were visible. Both eyes were pseudophakic. Posterior segment of the left eye showed dense vitritis, with 2 areas of retinitis – superior nasal (Figure 2) and inferior nasal. No retinal breaks visible. Infective screen for HIV, Hepatitis B, and Hepatitis C were negative. Rapid Plasma Reagin (RPR) testing was non-reactive and Treponema Pallidum Particle was not detected. Serology for Toxocariasis was negative. Serum Toxoplasmosis antibodies IgM was negative, but IgG was positive at 3.584. Mantoux test was 13mm, but serum PCR for TB was negative. Vitreous tap was negative for CMV, HSV1, HSV2, and

VZV DNA. Vitreous PCR for toxoplasmosis was not available at the time.

He was started on oral Prednisolone 1 mg/kg od, which was tapered by 10 mg every 5 days, oral Bactrim (Sulfamethoxazole 800mg and Trimethoprim 160mg), and PredForte 4-hourly. He had a raised IOP of 23 mmHg and was started on Timolol. Upon follow-up, he responded well to the above treatment, and the oral Prednisolone and PredForte were tapered down. Oral Bactrim was continued. Visual acuity in the affected eye was 6/9 at 8 weeks post initiation of treatment.

However, after completion of the oral Prednisolone regimen, the patient noticed a reduction in vision, and 8 days later presented with a 360° exudative retinal detachment (RD) with a visual acuity of 6/18. Anterior chamber activity was 1-2+ with minimal vitritis. He was restarted on oral Prednisolone 1 mg/kg. He returned the following day with a sudden drop in visual acuity to perception of light, with a bullous RD involving the macula (Figure 3), which was confirmed with a B-scan. A trans pars plana vitrectomy (TPPV) with silicone oil was performed, no retinal break(s) seen intraoperatively. At one month post-op, he underwent another surgery for removal of silicone oil as he was found to have raised intraocular pressure. Three months post retinal detachment surgery, his best corrected visual acuity improved to 6/18 (Figure 4).

Two months later, vision in the affected eye reduced to counting fingers. A yellow central macular lesion was noted and subsequently developed into a fibrotic scar. This lesion was appeared at a different location from the previously described areas of retinitis. The optic disc appeared pale. An immune reaction was suspected and he was restarted on oral Prednisolone regime in a tapering manner (Figure 5). However the fibrotic scar remained the same but developed neovascularization

around the lesion (Figure 6). Choroidal neovascularization (CNV) was suspected and a fundus fluorescein angiography was performed which showed subfoveal leakage corresponding to the lesion shown in Figure 7. He was then given 3 consecutive intravitreal injections of Bevacizumab and his OCT (Figure 8) showed resolution of the subretinal fluid but his vision remained blurred at counting fingers.



Figure 1: Anterior segment showing resolving keratic precipitates.

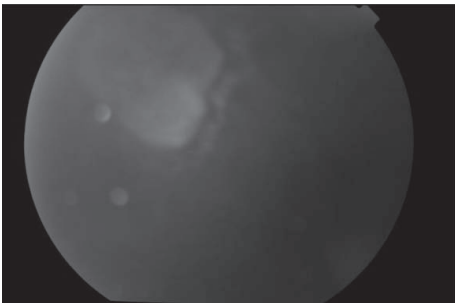


Figure 2: Fundus photo showing superior nasal lesion.

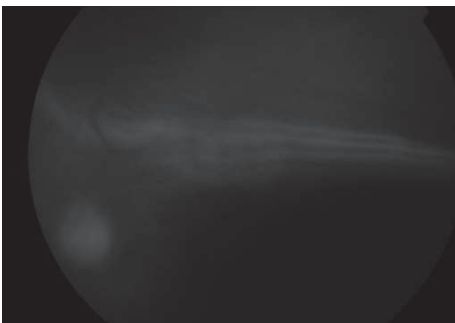


Figure 3: Retinal detachment with dense vitritis.

On the last follow-up, two years after the initial treatment for ocular toxoplasmosis, the retina is flat with no recurrence of disease and the subfoveal choroidal neovascularization remained inactive with no further improvement of vision.

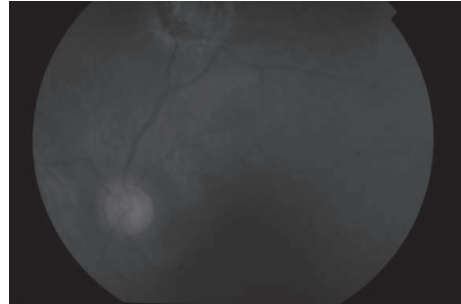


Figure 4: Fundus photo of affected eye 11 weeks post TPPV.

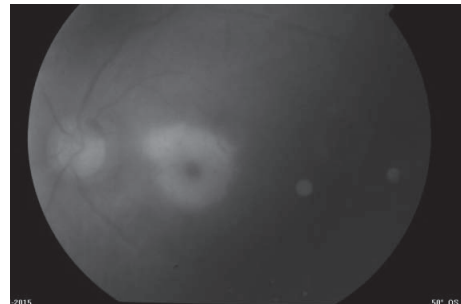


Figure 5: Fibrotic scar at macula.

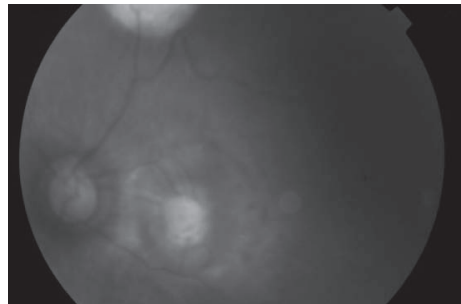


Figure 6: Foveal edema with surrounding neovascularization.

Discussion

Ocular toxoplasmosis, a disease caused by the parasite *Toxoplasma gondii*, an obligate intracellular protozoan. It is one of the most frequently identifiable causes of

uveitis worldwide. In fact, *Toxoplasma gondii* infection is the most common cause of infectious posterior uveitis in non-immunocompromised individuals, second only to cytomegalovirus retinitis in patients with HIV/AIDS.³ While cats are the definitive hosts, humans serve as intermediate hosts to *Toxoplasma gondii* and approximately 33% of the human population worldwide is infected by the parasite. Fortunately, ocular manifestations are generally found in only 2% of those infected.^{4,5}



Figure 7: A fundus fluorescein angiography showing subfoveal leakage.

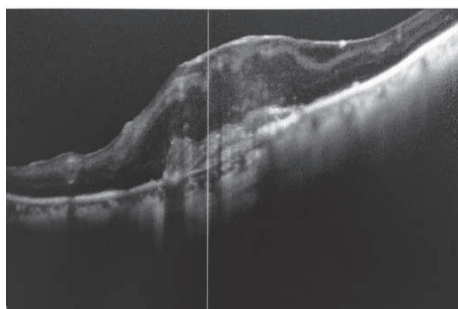


Figure 8: Heidelberg OCT of macula.

Typical presentation of ocular toxoplasmosis includes a characteristic finding of unilateral and focal retinochoroiditis with an adjacent healed retinochoroidal scar. Vitreous inflammation may also be present. Rarely, especially in patients with immune compromise, ocular toxoplasmosis presents atypically as aggressive retinal choroiditis.^{6,7} Patients with ocular toxoplasmosis often describe blurred or hazy vision and floaters, with absence of pain.

Up to 20% of patients have acute ocular hypertension at presentation.⁸ On fundus examination, most commonly there will be unilateral bright white-yellow retinal lesions. Retinal hemorrhages are usually absent. Significant vitritis is a common finding.⁸ Anterior chamber spill over may also occur.

Although diagnosis is most often made clinically, based on characteristic fundus lesions, laboratory investigations aid in confirming the diagnosis, especially for atypical presentations. An initially incorrect diagnosis with prolonged empiric treatment may be harmful by delaying appropriate treatment resulting in suboptimal visual outcomes. Use of corticosteroids without simultaneous antitoxoplasmosis treatment may result in more rapid progression of the chorioretinitis. Polymerase chain reaction amplification of toxoplasmic DNA is faster than culture, requiring only small amounts of intraocular fluid. However, an intracellular organism such as *Toxoplasma gondii* would not usually be expected to be floating freely in intraocular fluid.⁹ IgM antibodies will rise early post-infection and remain detectable for less than one year, while IgG antibodies will appear within the first two weeks post-infection and remain detectable for life. Because these antibodies are highly sensitive markers of the disease state, antibody testing is helpful in ruling out toxoplasmosis when the result is negative.¹⁰

Ocular Toxoplasmosis presenting typically is a self-limiting disorder, usually resolving within 6 weeks to 2 months. It is not established that antibiotics improve short-term disease course or long-term visual outcomes in the immunocompetent persons compared to observation or placebo¹¹. Bactrim (trimethoprim-sulfamethoxazole) 160/800 mg twice daily has been shown to be equivalent to the traditional triple-therapy regimen of Pyrimethamine, Sulfadiazine, and Folinic acid. Level I ev-

idence backs intermittent treatment every few days with Bactrim to significantly reduce the risk of recurrence of retinochoroiditis.¹² Concomitant prednisolone therapy of 0.5 to 1 mg/kg daily is also often used to reduce inflammation, although there is limited evidence from randomized clinical trials demonstrating their effectiveness as an adjuvant therapy.^{13,14} However, steroids should not be used as monotherapy (without antibiotics), or in the immunocompromised patient due to the high probability of inducing fulminant retinochoroiditis.¹⁵

A study by Faridi et al of 35 eyes of 28 patients diagnosed with ocular toxoplasmosis showed that 11.4% of patients developed RD which led to severe vision loss despite successful RD repair.¹⁶ A study of 150 patients with ocular toxoplasmosis by Bosch-Driessen et al showed that 6% had RD and a further 5% had retinal breaks. It was noted that intraocular inflammation in eyes preceding the RD or retinal breaks was severe. It was also noted that the frequency of myopia was significantly higher in eyes with retinal detachment and breaks as compared to those without detachment or breaks.¹⁷ The patient described in this case is not known to be myopic although both eyes were pseudophakic, and the inflammation sustained during his attack of ocular toxoplasmosis was no more severe than what was usually expected. Despite this he still developed retinal detachment followed by choroidal neovascularization following the initial acquired retinitis due to toxoplasmosis.

Choroidal neovascularization is a rare complication of ocular toxoplasmosis, which usually arises secondary to retinochoroiditis and macular scarring.¹⁸ Increased expression of vascular endothelial growth factor (VEGF), compromise in the Bruch membrane, and inflammation secondary to toxoplasmosis infection may contribute to the formation of neovascular disease.¹⁹ A study by Rasier et al showed

that intravitreal VEGF concentrations were significantly elevated in vitreous samples of patients with RD.²⁰ The CNV lesion in the patient described in this case is located at the macula, away from the original 2 lesions of retinitis – superior nasal and inferior nasal. It may be postulated that the CNV may be a complication of the inflammation from the original insult of retinitis, or secondary to the operated RD, or a combination of both. *Toxoplasma gondii* has been shown to express VEGF in tissue culture. This justifies specifically targeting VEGF when treating CNV in ocular toxoplasmosis. Benevento et al showed that CNV lesions occurring as a complication of ocular toxoplasmosis were successfully treated with intravitreal Ranibizumab and antiparasitic therapy.²¹ Korol et al showed that intravitreal Aflibercept has been shown to have a positive clinical effect and was well tolerated for the treatment of CNV associated with chorioretinitis including those secondary to *Toxoplasma gondii*.²² Verteporfin photodynamic therapy (V-PDT) has been shown to be effective and safe in treating subfoveal choroidal neovascularization associated with ocular toxoplasmosis.²³ Adan et al reported a case of ocular toxoplasmosis with subfoveal choroidal neovascularization. The patient underwent pars plana vitrectomy and submacular surgery with subsequent improvement of visual acuity and resolution of metamorphopsia.²⁴ The patient in this case developed what was thought to be an immune reaction 2 months post retinal detachment surgery. Although he was treated with Bactrim and Prednisolone, he still progressed to develop choroidal neovascularization. Intravitreal Bevacizumab was used in this case and the neovascularization resolved after 3 doses.

This case illustrates a case of ocular toxoplasmosis in an immunocompetent individual. He was treated adequately with Bactrim and Prednisolone yet subsequently

still developed RD followed by subfoveal CNV. Despite surgical intervention for the retinal detachment and anti-VEGF treatment for the choroidal neovascularization, his vision unfortunately remains poor.

Conclusion

It is important for vigilant examination of patients with ocular toxoplasmosis to aid early identification of potential complications like retinal detachment and choroidal neovascularization. One needs to be aware of such devastating complications as in some unfortunate cases as demonstrated here, despite adequate intervention, the outcome remains poor.

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The outcome of upperlid lowering by using auricular cartilage as a spacer for thyroid-related upper eyelid retraction

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Objective: To review the outcome of upper lid lowering by using auricular cartilage as the spacer for thyroid-related upper eyelid retraction.

Methods: A case series comprised of 23 eyes which were diagnosed with medium/severe graded thyroid-related upper eyelid retraction. The patients were operated at Ho Chi Minh City Eye Hospital, using auricular cartilage as the spacer to lower upper lid. Data were collected before and during 6 months after the surgery.

Results: More than 90% of preoperative symptoms improved: good upper lid lowering (95.65%), lagophthalmos improved (100%). Only 13.04% of eyes remained lateral upper eyelid retraction. Complications: keratopathy (8.68%); graft extrusion (0%); ptosis (0%). Only 1 eye was recurrent (4.34%).

Conclusion: Upper lid lowering by using auricular cartilage as the spacer is a safe and effective method to treat thyroid-related upper eyelid retraction. This method brings good cosmetic results and improves keratopathy because of upper lid retraction.

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

Keywords: upper lid lowering, auricular cartilage

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Introduction

Upper eyelid retraction is defined as being present when the upper eyelid is above the normal position in primary gaze. At the normally straight position of the eye, 2 mm is covered by the upper lid from the superior limbus of the cornea. Upper lid retraction can have many causes, the most common of which is thyroid eye disease. In dysthyroid upper eyelid retraction, causative factors of the disease include sympathetic stimulation of Muller's muscle and increased tone and over-activity

of levator-superior rectus muscle complex secondary to fibrosis of the inferior rectus.^{1,2} Upper eyelid retraction surgical correction not only improves the cosmetic aspect of the patients, removing their ferocious look due to lid lowering, but protects the cornea as well. The surgery is scheduled when the disease condition is stable, the patient's thyroid function is normal, and the upper eyelid condition has been stable for at least 6 months. There are many approaches to treating upper eyelid retraction. Anterior approaches consist of levator muscle recession with or without adjustable sutures; Mullerectomy or Mullerotomy; levator muscle marginal myotomy; stepped complete palpebral incision; and Z-plasty. Muller and levator

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muscle posterior (conjunctival) approaches were also reported and adjusted.^{1,3-5} These approaches vary in initial and postoperative effectiveness despite the stable underlying thyroid disease. There is a hypothesis indicating that these approaches make a cavity in the upper eyelid which enhances the wound healing process which in turn stimulates the retraction. Hence, with a spacer placed as a wedge between the levator aponeurosis and the upper lid tarsal plate, the retraction could be restrained.⁷ In this study, we evaluated the effectiveness of the surgery in thyroid-associated upper eyelid retraction using auricular cartilage as a spacer. This is an easily taken autologous material, which rarely causes complications and cosmetic deformation at the cartilage position and on itself. The cartilage is flexible but strong enough to maintain the form and the postoperative lid lowering effectiveness.

Methods

We did a prospective study on 17 patients from 24 to 72 years old, consisting of 8 males and 9 females; in total, there are 23 eyes investigated, 9 right eyes and 14 left ones. Among those, 6 patients were operated on both eyes, and the other 11 patients were operated on one eye.

The selection criteria included patients with moderate or severe thyroid-associated upper eyelid retraction being stable for at least 6 months, and with settled thyroid function.

Upper eyelid retraction classification is based on MRD (Margin Reflex Distance):

- Mild retraction: $MRD \leq 5$ mm
- Moderate retraction: $5 \text{ mm} < MRD \leq 7$ mm
- Severe retraction: $MRD > 7$ mm⁶

All patients were examined before and after surgery by the same ophthalmologist and were operated on by the same surgeon. Medical history regarding retraction was carefully explored and documented with cornea-related symptoms caused by wid-

ened palpebral aperture like dry eye, irritated feelings, burning and scratchy eyes, a feeling of something in the eye, excess watering, blurred vision, or photophobia. Preoperative assessment was carried out to evaluate the degree of upper eyelid retraction, the measure of palpebral aperture, the corneal condition and other thyroid-associated eye manifestations, if present. Patients were examined to evaluate thyroid function including fT3, fT4, TSH, TRAb (TSH receptor antibody); thyroid ultrasound; and the enlargement of recti muscles and optic nerve by orbital ultrasound and CT scans. An eyelid lengthening surgery was done after the surgery on orbital decompression and strabismus in case of operative indication.

SURGERY PROCEDURE

1. Posterior auricular cartilage harvesting (Figure 1)



Figure1: Posterior auricular cartilage harvesting

- Subcutaneously anaesthetize posterior auricular area
- Skin incised and dissected to expose the sub-perichondrium plane
- Use blade No.11 and compatible scissors to harvest the cartilage with the size: 25 mm in length * (MRD – 2.5 mm) in height
- Close the postauricular incision with a 7.0 silk suture.

2. Cartilage transplantation technique

- Evert the upper eyelid
- Inject anesthetic solution to the fornix of conjunctiva (Figure 2)

-Dissect conjunctiva from superior eyelid tarsal border and Muller's muscle to the upper margin (Figure 3)



Figure 2: Injection of anesthetic solution to the fornix of conjunctiva



Figure 3: Dissection of conjunctiva from superior eyelid tarsal border and Muller's muscle to the upper margin

-Use fine toothed forceps to grasp the complex of levator muscle and Muller's muscle, and remove it from superior tarsal border (Figure 4)

-Suture the auricular cartilage between the tarsus and levator muscle – Muller's muscle by 6.0 Vicryl suture (Figure 5)

-Suture the conjunctiva back to superior eyelid tarsal border to line the interior surface of the transplanted cartilage.

Postoperatively, patients were evaluated after 1 week, 1 month, 3 months and 6 months. Important points of follow-up examination include: upper lid lowering degree; palpebral aperture degree; the healing of corneal disease or other preoperative accompanied symptoms; and com-

plications. Cosmetic factors such as two eye symmetries, height of the upper lid crease, and the cartilage area were carefully observed upon re-examination. Lid contour was evaluated mainly on whether the normal curvature of the lid was preserved. Regarding the spacer, follow-up examination focused on the question of if the spacer was rejected or contracted.

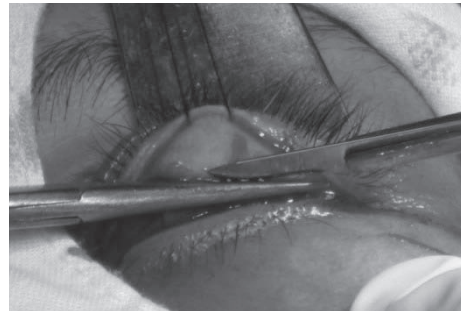


Figure 4: Removal of the complex of levator muscle and Muller's muscle from superior tarsal border



Figure 5: Suture of the auricular cartilage between the tarsus and levator muscle – Muller's muscle

Evaluation standard

1. Evaluate the orbital protective functional recovery: postoperative eyelid lowering degree, at every follow-up examination (1 month, 3 months and 6 months) and the recurring rate by MRD index (marginal reflex distance).

-Acceptable: $3.5 \text{ mm} \leq \text{MRD} \leq 5 \text{ mm}$

-Overcorrected: $2.5 \text{ mm} \leq \text{MRD} < 3.5 \text{ mm}$

-Undercorrected: $\text{MRD} > 5 \text{ mm}$

-Recurrence is defined by having MRD 1-month post-op > 5 mm.

2.Evaluate cosmetic recovery with two eyelid apertures symmetry through dMRD index (the difference index in lid apertures between left and right side)

-Good: $0 \text{ mm} \leq \text{dMRD} < 1 \text{ mm}$

-Satisfied: $1 \text{ mm} \leq \text{dMRD} < 2 \text{ mm}$

-Unacceptable: $\text{dMRD} \geq 2 \text{ mm}$

3.Evaluate corneal symptoms preoperatively and postoperatively: basing on clinical signs and BUT diagnostic test (tear film break-up time)

Results

17 patients comprised of 8 men and 9 women with 23 eyes with thyroid-associated eyelid retraction at moderate ($5 \text{ mm} < \text{MRD} \leq 7 \text{ mm}$) and severe ($\text{MRD} > 7 \text{ mm}$) degree were operated by auricular cartilage transplantation to lowering the upper lid at Ho Chi Minh City Eye Hospital. Results about orbital protective function are summarized in Figure 6. Results about cosmetic recovery are presented in Figure 7

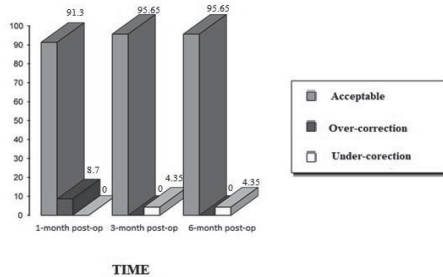


Figure 6: Results about orbital protective function

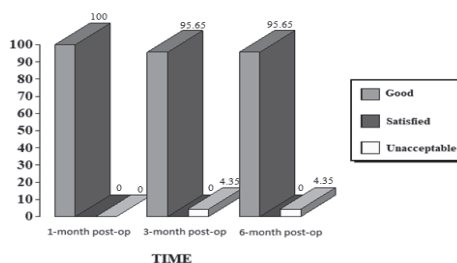


Figure 7: Results about cosmetic recovery

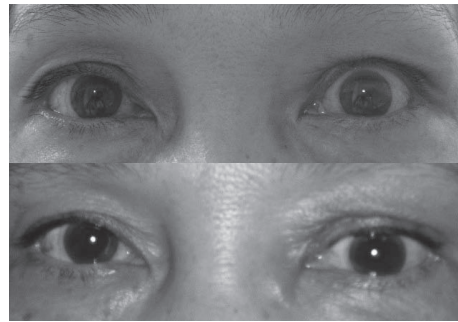


Figure 8: Upper eye: Thyroid-associated upper lid retraction (Upper image: pre-op; Lower image: 6 months post-op lid lengthening – Good result)



Figure 9: Both eyes: Improved corneal condition after lid lengthening surgery (Upper image: Right eye: 1-week post, Left eye: pre-op; Lower image: 6 months post-op lid lengthening)

In 3 eyes with remaining temporal eyelid retraction, 2 were corrected by additional levator dissecting operation in temporal canthus area, so this condition was well improved. High lid crease complications were relatively common, up to 43.48%; however, these complications increasingly improved over time, with continued follow-up.

BUT and other symptoms of postoperative palpebral aperture corneal illness were completely improved.

Table 1: Remaining limitations after 6 months post-operatively

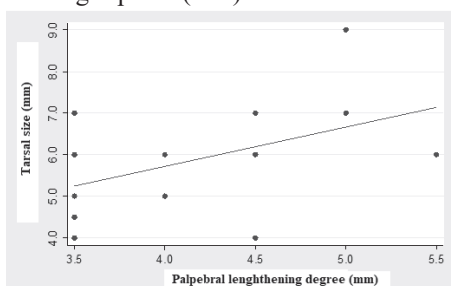
Post-op Limitations	N	%
0.5 mm mild eyelid aperture	4	17.39
High lid crease, thick lid	10	43.48
Lid curvature abnormality	3	13.04
Mild temporal eyelid retraction	3	13.04

Table 2: Postoperative complications

Complications	N	%
Superior marginal keratitis +/- ulceration	2	8.69
Blepharitis	8	34.78
Granulomatous conjunctivitis	1	4.35

Other complications (included eyelash loss; dry eye; graft rejection; wound slowly or barely healing) were undocumented in follow-up period (6 months since operation). Auricular cartilage harvesting area healed well, not affecting patients' comfort regarding the function and cosmetic aspects. When exploring the correlation between the cartilage spacer size and the palpebral lengthening degree, the Spearman correlation coefficient is 0.8112 ($p=0.0000$).

Correlation equation: Palpebral lengthening degree (mm) = $-0.148 + 0.750 \times$ size of cartilage spacer (mm)

**Figure 10:** Scatter plot for the palpebral lengthening degree

Discussion

Whether being a separate manifestation or accompanying with bulging eye, lower

eyelid retraction, thyroid-associated upper eyelid retraction still significantly affects the eyelid's cosmetic aspect and its corneal protective function. There are many corrective surgeries for this upper eyelid condition depending on severity, accompanying illness, and the period of thyroid-associated orbital disease. The classic methods like levator muscle recession with or without adjustable suture; Mullerectomy or Mullerotomy; marginal myotomy; stepped complete palpebral incision; and Z-plasty have been practiced for a relatively long time because of their effectiveness in upper eyelid retraction at a mild and moderate degree. At the severe degree, the effectiveness of these methods has not been supported. Many opinions indicate that these methods made a cavity in upper eyelid, which enhanced the wound healing process and stimulated retraction. Consequently, with a spacer placed between the levator aponeurosis and the upper lid tarsal plate as a wedge, the retraction could be limited.⁷ This is the premise of the research of eyelid lengthening methods using spacers. The many materials that can be used are sclera; nasal cartilage; the other eye's tarsal plate; hard palate mucous membrane, and

more.^{6,7} However, there have been many issues such as rejection; spacer retraction; complications at the cartilage harvesting area; and the complicated and time-consuming techniques of harvesting those materials. The ideal spacer must bring out a predictable result, be stable and have few complications. Auricular cartilage is an autologous material that doesn't need complicated technique or much time to harvest. Moreover, auricular cartilage is both elastic and hard enough to be a wedge for creating a stable shape for the eyelid. For all the above reasons, we proceeded to study the primary effectiveness of the operation using auricular cartilage as a wedge on thyroid-associated upper lid retraction cases from moderate to severe.

In this research, we realized that a palpebral lengthening effect was achieved on over 95.65% of patients; the recurrent rate was very low, only 4.34% (1 in 23 eyes). In addition, the rate of good cosmetic requirements in eye symmetry was very high, 95.65%; unsatisfied rate was 0%; and unacceptable rate was only 4.34% (the above case has recurrent retraction). In these surgeries, because the sizes of cartilage spacers were calculated precisely pre-op, patients did not need to sit up many times to evaluate the lid lengthening degree as other previous methods. This is another convenience of this operative method.

Besides, in the collected reference documents, we have not found any information mentioning about the change in eyelid lengthening degree as the size of the auricular cartilage spacer varied. Hence, we studied the correlation between the size of the cartilage spacer and the palpebral lengthening degree 6 months postoperatively and got the Spearman correlation coefficient of 0.8112 with p -value of 0.0000. The connection between these two variables are also addressed in the following regression equation:

Palpebral lengthening degree (mm) =

$-0.148 + 0.750 \times \text{cartilage spacer size (mm)}$
In this equation, we made regression between these two variables: the palpebral lengthening degree, which is calculated by the difference between the preoperative MRD (marginal reflex distance) and 6-month postoperative MRD; and the size of auricular cartilage spacer.

Prob > F of 0.0000 showed that the model can be expressed for population with significance level of 5%.

And, the Squared correlation coefficient (R-squared) = 0.7163 = 71.63% told that the size of cartilage spacers could explain for 71.63% of the changes in the lengthening degree after 6 months.

Regarding complications, the most serious observed was superior marginal keratitis and ulceration (4.34%), and another case had a less serious complication: superior marginal superficial punctate keratitis. In our opinion, the cause of these complications was the fact that these were our first cases in the study, and we did not preserve the conjunctiva to cover the cartilage spacer; in the later cases with conjunctiva covering the spacer, there were totally no affected areas on the cornea. Moreover, there was still one granulomatous inflammation that responded well to the steroid eye drops. Blepharitis complications were seen in 34.78% of cases.

Conclusion

Use of external auricular cartilage as a wedge between levator aponeurosis and the upper lid tarsal plate seems to be the ideal method to correct thyroid-associated upper eyelid retraction of a moderate to severe degree because of high effectiveness, low recurrent rate, and few mild complications. However, the study is preliminary, and the sample number is not large enough to result in statistically significant conclusions.

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Infective keratitis in advanced glaucoma patients

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Background: To describe a case series of infective keratitis in patients with advanced glaucoma in Selayang Hospital, Malaysia.

Methods: This is a descriptive, retrospective case series. Data from January 2013 to December 2017 was traced from hospital database and analyzed.

Results: A total of 17 eyes of 16 patients was included in this series. Seven were males and nine were females. Mean age group was 64 ± 12 years old (range 48 to 93 years old). Twelve patients had underlying diabetes mellitus. Seven patients (44%) had primary glaucoma (Six POAGs and one PACG), while nine patients (56%) had secondary glaucoma, of which six were due to rubeosis iridis. All patients had premorbid vision of counting fingers or worse. Thirteen patients (81%) were on long term topical anti-glaucoma treatment prior to the development of infective keratitis. Most of the patients had poor IOP control at the time of diagnosis. Painful red eyes were the main presenting symptoms. Corneal scrapings were positive in nine (64.3%) out of the fourteen cases, in which three were *Pseudomonas aeruginosa*, one *Klebsiella* sp., three *Streptococcus* sp., and three others had mixed growth. Majority of the cases were treated medically, but three eyes required evisceration.

Conclusion: Diabetes mellitus, uncontrolled IOP, long term topical anti-glaucoma drops and poor premorbid vision are risk factors for developing infective keratitis in advanced glaucoma patients. Infective keratitis can lead to significant morbidity in this group of patients whose quality of life is already poor.

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Introduction

Glaucoma is a leading cause of visual impairment and irreversible blindness globally.¹ It can lead to significant morbidity and affect patients' quality of life. Patients

who are blind from advanced glaucoma can also develop other complications, including infective keratitis. Infective keratitis is a very serious eye condition that can lead to significant corneal scarring and vascularization, or in worst scenarios, corneal perforations which warrant evisceration.

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Purposes

1. To describe the incidence of infective keratitis in patients with advanced glaucoma in Selayang Hospital, Malaysia.

- 2.To determine the risk factors for infective keratitis in this group of patients.
- 3.To determine the causative organisms causing infective keratitis in this group of patients.
- 4.To determine the ocular outcomes of these patients.

Methods

This is a descriptive retrospective case series done from the period between January 2013 and December 2017 in Selayang Hospital, Malaysia. Data collection was done by tracing the electronic patient records and ward admission census. Patients' age, gender, race, diagnosis, glaucoma treatment, visual acuity before developing infective keratitis (premorbid visual acuity), vision at presentation and presenting intraocular pressure (IOP) were recorded. Microorganism culture results and outcome of the treatment were also included in the data collection.

Results

A total of 17 eyes of 16 patients was included in this series. Out of these, 10 patients were Chinese; five were Malay and one was Indian. There were seven males (44%) and nine females (56%). Mean age group was 64 ± 12 years old (range 48 to 93 years old). Ten cases involved the right eye while five cases involved the left eye, one patient had bilateral eye involvement. Twelve patients had underlying diabetes mellitus, twelve patients had hypertension while three patients had end stage renal disease. Seven patients (44%) had primary glaucoma (Six cases of primary open angle glaucoma and one case of primary angle closure glaucoma), whereas nine patients (56%) had secondary glaucoma, of which six were due to rubeotic glaucoma secondary to proliferative diabetic retinopathy (PDR).

All patients had a premorbid vision of counting fingers or worse (counting fingers,

hand movement, perception of light or no perception of light). Thirteen patients (81%) were on long term topical anti-glaucoma treatment prior to the development of infective keratitis. Most of the cases (12 patients) had poor IOP control at the time of diagnosis of infective keratitis. Almost all patients presented with painful red eyes. Eleven cases presented with hypopyon, three cases developed corneal melting and perforation (one patient had bilateral eye corneal perforations). Corneal scrapings were sent in 14 cases and out of these, nine (64.3%) were positive for organisms and five (35.7%) had no growth. Of the positive cultures, all were due to bacterial pathogens; four (28.6%) were Gram-negative bacteria (three cases of *Pseudomonas aeruginosa* and one case of *Klebsiella* sp.), three (21.4%) were Gram-positive (*Streptococcus* sp.) while the other two (14.3%) had mixed growth.

All cases were treated with empirical topical antibiotics; three cases were treated with topical anti-fungals (amphotericin B 0.15% and fluconazole 0.2%) and systemic anti-fungal (oral fluconazole 200 mg OD) based on the clinical presentation (fluffy edged infiltrates with endothelial plaques). One patient developed endophthalmitis and was treated with intravitreal antibiotics (vancomycin 1mg in 0.1ml and ceftazidime 2 mg in 0.1ml). Majority of the cases (12 patients) were prescribed a combination of topical ceftazidime 5% and fortified gentamicin 0.9%. Three patients were started on fluoroquinolone monotherapy of either topical moxifloxacin 0.5% or ciprofloxacin 0.3%. Systemic antibiotics (intravenous or oral ciprofloxacin) were started in four patients as they developed corneal perforation and endophthalmitis. Despite intensive anti-microbial therapy, three eyes had to be eviscerated following corneal perforation and melting. Eight cases had healed from infective keratitis with corneal scarring and vascularization, three cases

developed decompensated corneas while four cases were lost to follow up.

Discussion

Glaucoma is one of the leading causes of visual impairment and irreversible blindness worldwide, with an estimated 8.4 million people getting blindness from glaucoma.¹ Infective keratitis can develop in patients with advanced glaucoma, leading to significant morbidity and further affecting patients' quality of life. This case series describes the incidence of infective keratitis in patients with advanced glaucoma in Selayang Hospital, Malaysia.

In this series, Gram-negative organisms were the commonest organism cultured; there were three cases of *Pseudomonas* infection and a case of *Klebsiella* infection, followed by three cases of Gram-positive organisms, all of which were *Streptococcus* infection. There were no fungal organisms which were cultured. Interestingly, there are geographic variations in bacterial keratitis, with Paraguay reporting the highest number of Staphylococcal infections (79%), Bangkok reporting the highest prevalence of *Pseudomonas* infections (55%), and Tamil Nadu more prevalent with Streptococcal infections (47%).²

Diabetes mellitus seems to be an important causative factor for corneal ulcers. Diabetes can lead to poor tear film quality, ocular surface disease, diabetic keratopathy and neurotrophic keratopathy.³ Diabetic keratopathy can lead to fragile corneal epithelium and poor healing of epithelial defects. This condition is made worse by corneal hypoesthesia as seen in neurotropic keratopathy, which ranges from punctate keratopathy, epithelial irregularity to epithelial breakdown and even corneal ulcers which can melt and perforate.³ On the other hand, endothelial cell dysfunction could lead to corneal decompensation and development of bullous keratopathy.³

Contamination of anti-glaucoma drops

may also contribute to infective keratitis. A study done by Teuchner et al. showed that the contamination rate of topical anti-glaucoma is significantly higher than of antibiotics or anesthetic eye drops. In the same study, it was also found that the tip of the medication bottle was more frequently contaminated as compared to the eye drops themselves.⁴ Another study also showed that advanced glaucoma patients with poor vision or severe visual field defects had higher failure rates of eye drop instillation.⁵ Frequently, the tip of medication bottles touches the bulbar conjunctiva, cornea, eyelid or eyelashes during drug instillation, and this might lead to unintentional injury of the ocular surface.⁵ Together with the contamination of eye drops, they may contribute to infective keratitis especially in this group of patients. Therefore, the presence of an assistant to help instill eye drops could be beneficial.

Another causative factor is the long-term use of topical anti-glaucoma eye drops, which can lead to tear film instability and ocular surface disorders.⁶ A study has shown that latanoprost causes significant reduction in tear break-up time, and brimonidine causes significant reduction in the basal secretion of tears.⁶ In another study done by Baratz et al., chronic use of topical anti-glaucoma eye drops also leads to a reduction in the number and density of corneal sub-basal nerve fibers, which could worsen cornea hypoesthesia as described above.⁷

In this series, most of the affected patients had suboptimal IOP control despite being on medications. Uncontrolled intraocular pressure could lead to corneal decompensation and hence predispose the patients to corneal ulcers. In a study by Martin et al., the authors showed high success rates of cyclodiode laser treatment for IOP reduction and pain relief in blind glaucomatous eyes.⁸ Hence in eyes with poor visual prognosis, cyclodiode laser treatment could be

performed for IOP control and pain relief, as well as to reduce the need for topical anti-glaucoma eye drop usage.

Severe bacterial keratitis warrants intensive antibiotic therapy, which usually consists of topical fluoroquinolone monotherapy or aminoglycoside-cephalosporin combination. Prompt empirical treatment is usually required to cover for both gram-positive and gram-negative pathogens while waiting for culture and sensitivity results. In this series, most of our patients were treated with a combination of fortified aminoglycoside-cephalosporin, with a few treated with fluoroquinolone monotherapy. Interestingly, a meta-analysis⁹ comparing monotherapy and combination therapy has shown no significant difference in their efficacy. Fluoroquinolones were shown to significantly reduce ocular discomfort and rate of chemical conjunctivitis compared to combination therapy, while fortified combination therapy was said to cause increased corneal irritation and delayed corneal epithelialization.⁹ The risk of corneal perforation between the two groups did not differ significantly. However, topical fluoroquinolone especially ciprofloxacin has an increased risk of white precipitate formation.⁹

Conclusion

Diabetes mellitus, suboptimal IOP control, long term topical anti-glaucoma drops and poor premorbid vision are the risk factors for developing infective keratitis in patients with advanced glaucoma. Infective keratitis can lead to significant morbidity in advanced glaucoma patients whose quality of life are already poor. Hence, prevention is better than cure and prompt treatment of infective keratitis is the key.

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Table 1: Demographic Data of Patients

Case	Age (years)	Sex	Race	Co-morbid	Eye	Ocular Diagnosis	Topical Antiglaucoma	Pre-morbid vision
1	53	M	Malay	DM HPT	OD	Rubeotic glaucoma secondary to PDR	Latanoprost Brimonidine	NPL
2	64	F	Chinese	DM HPT	OD	Aphakic glaucoma	Timolol Latanoprost	HM
3	69	F	Malay	nil	OD	Advanced PACG	Timolol Latanoprost	PL
4	66	F	Chinese	nil	OD	Advanced POAG	Timolol Latanoprost Brimonidine Dorzolamide	PL
5	50	F	Malay	DM	OD	Advanced POAG	Timolol Latanoprost Brimonidine Dorzolamide	CF 1ft
6	93	F	Malay	nil	OS	Advanced POAG	NIL	NPL
7	69	M	Chinese	DM HPT	OD	Advanced POAG	Timolol Latanoprost Brimonidine	NPL
8	50	M	Malay	DM HPT	OS	Rubeotic glaucoma secondary to PDR	Timolol Latanoprost	HM
9	78	F	Chinese	HPT IHD	OD	Advanced POAG	Timolol Bimatoprost	PL
10	48	M	Chinese	DM HPT ESRD	OD	Rubeotic glaucoma secondary to PDR	Brimonidine Dorzolamide	NPL
11	63	F	Indian	DM HPT	OS	Rubeotic glaucoma secondary to PDR	Timolol Latanoprost	NPL
12	52	M	Chinese	DM HPT	OS	Rubeotic glaucoma secondary to PDR	Timolol Bimatoprost	HM
13	62	M	Chinese	DM HPT ESRD	OU	Uveitic glaucoma	NIL	OD NPL OS CF 1ft
14	62	F	Chinese	DM HPT ESRD	OD	Rubeotic glaucoma secondary to PDR	Timolol Latanoprost Brimonidine	HM
15	62	M	Chinese	DM HPT	OS	Secondary glaucoma post complicated cataract surgery	Timolol Latanoprost Brimonidine Dorzolamide	HM
16	81	F	Chinese	DM, HPT CRD	OD	Advanced POAG	NIL	NPL

Abbreviations

CRD : Chronic Renal disease
DM : Diabetes Mellitus
ESRD : End stage renal disease
HPT : Hypertension

IHD : Ischemic heart disease
PDR : Proliferative diabetic retinopathy
POAG : Primary open angle glaucoma
PACG : Primary angle closure glaucoma

Table 2: Clinical presentations of patients

Case	Presenting Vision	Presenting IOP (mmHg)	Symptoms	Signs
1	NPL	38	Pain and redness x 5/7	Hypopyon, dense stromal abscess
2	HM	13	Pain and redness x 3/7	Paracentral infiltrate, hypopyon
3	PL	33	Pain, redness, discharge x 3/7	Paracentral infiltrate
4	NPL	27	Pain and discharge x 4/7	Hypopyon, corneal melting
5	CF 1ft	26	Pain and redness x 1/52	Paracentral infiltrate, hypopyon
6	NPL	23	Pain and discharge x 1/12	Perforated corneal ulcer
7	NPL	27	Pain and redness x 2/52	Central infiltrate, hypopyon
8	HM	27	Pain and redness x 3/7	Paracentral infiltrate, endothelial plaque
9	PL	20	Pain and redness x 1/52	Hypopyon, central infiltrate
10	NPL	8	Pain x 3/7	Total hypopyon, corneal thinning
11	NPL	49	Pain and redness x 3/7	Central infiltrate, hypopyon
12	HM	8	Redness and discharge x 4/7	Paracentral infiltrate, hypopyon
13	OD NPL OS PL	30	Pain and redness x 1/52	Perforated corneal ulcer
14	NPL	30	Pain and discharge x 2/52	Paracentral infiltrate, hypopyon
15	PL	8	Redness and discharge x 3/7	Central infiltrate, endothelial plaque
16	NPL	36	Redness and discharge x 2/7	Central infiltrate, hypopyon

Table 3: Treatments and outcome of patients

Case	Microorganism culture	Treatment	Final Vision	Outcome
1	Streptococcus group C	Gtt. CAZ 5% Gtt. GEN 0.9%	NPL	Corneal scar, vascularization
2	Pseudomonas aeruginosa	Gtt. CAZ 5% Gtt. GEN 0.9%	HM	Decompensated cornea
3	Klebsiella sp.	Gtt. CAZ 5% Gtt. GEN 0.9%	NPL	Corneal scar, vascularization
4	Pseudomonas aeruginosa	Gtt. CAZ 5% Gtt. GEN 0.9%	-	Eviscerated
5	No growth	Gtt. MXF 0.5%	CF 2ft	Corneal scar
6	Not sent	Gtt. CIP 0.3% Tab. CIP 250mg BD	NPL	Tarsorrhaphy done Loss to follow up
7	No growth	Gtt. CAZ 5% Gtt. GEN 0.9% Gtt. AMB 0.15% Gtt. FLC 0.2%	NPL	Corneal scar, vascularization
8	No growth	Gtt. CAZ 5% Gtt. GEN 0.9% Gtt. AMB 0.15% Gtt. FLC 0.2% IVit VAN 1mg in 0.1ml IVit CAZ 2mg in 0.1ml Tab. FLC 200mg OD Tab. CIP 500mg BD	HM	Endophthalmitis, Decompensated cornea
9	Pseudomonas aeruginosa	Gtt. CAZ 5% Gtt. GEN 0.9%	NPL	Corneal scar, vascularization
10	Mixed growth	Gtt. CAZ 5% Gtt. GEN 0.9% IV CIP 200mg OD	NPL	Corneal perforation, loss to follow up
11	Streptococcus pneumoniae	Gtt. CAZ 5% Gtt. GEN 0.9%	NPL	Corneal scar, vascularization
12	Not sent	Gtt. CXM 5% Gtt. GEN 0.9% Tab. CIP 750mg BD	CF 1ft	Loss to follow up
13	No growth	IV CIP 250mg OD Gtt. MXF 0.5%	-	BE eviscerated
14	No growth	Gtt. CAZ 5% Gtt. GEN 0.9%	NPL	Bullous keratopathy, decompensated cornea
15	Mixed growth	Gtt. CAZ 5% Gtt. GEN 0.9% Gtt. AMB 0.15% Gtt. FLC 0.2% Tab. FLC 200mg OD	HM	Corneal scar, vascularization
16	Streptococcus pneumoniae	Gtt. CAZ 5% Gtt. GEN 0.9%	NPL	Corneal scar, vascularization

Abbreviations

AMB : Amphotericin B
CAZ : Cefotaxime
CIP : Ciprofloxacin
CXM : Cefuroxime

FLC : Fluconazole
GEN : Gentamicin
Gtt : Gutta
IV : Intravenous

IVit : Intravitreal
MXF : Moxifloxacin
Tab : Tablet
VAN : Vancomycin

Is endocyclophotocoagulation (ECP) effective after failed glaucoma drainage device (GDD) surgery? The Malaysian experience

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Purpose: To investigate the efficacy, survival time and safety profile of endoscopic cyclophotocoagulation (ECP) in patients with failed primary glaucoma drainage device (GDD).

Material and methods: A retrospective case review of ten patients with primary GDD implantation who underwent ECP from July 2013 to April 2018. Ten eyes of 10 patients were included. Indication of ECP was failure to achieve target IOP with maximal tolerated medical therapy despite the GDD implantation. ECP were performed by a single surgeon over at least 270 degrees and the subjects were followed up to 1 year. Main outcome measures were mean reduction in IOP and anti-glaucoma medications at 1, 3, 6 and 12 months. The visual acuity and complications were also documented.

Results: Mean IOP at baseline, 1, 3, 6 and 12 months were 17.7 ± 3.74 mmHg, 18.1 ± 8.1 mmHg, 18.1 ± 6.1 mmHg, 16.5 ± 5.9 mmHg, and 15.2 ± 4.8 mmHg respectively. Although the IOP post ECP was in the downwards trend, it was not statistically significant ($p=0.916$). Mean difference in number of anti-glaucoma medications were 1.40, 1.44, 1.38, and 1.5 at baseline, 1, 3, 6 and 12 months respectively, which was statistically significant up to 6 months ($p=0.036$). One patient required repeat ECP due to uncontrolled high IOP and another had recurrent rhegmatogenous retinal detachment. No other complications encountered.

Conclusion: ECP is a useful and safe surgery in managing refractory glaucoma with inadequate IOP control post primary GDD implantation.

Conflict of Interest: There is no conflicting relationship exists for any author.

Key words: Endocyclophotocoagulation, ECP, Tube-shunt, Glaucoma drainage device, GDD, failed GDD

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Introduction

Glaucoma drainage device (GDD) has increasingly gained its popularity to treat refractory glaucoma or when other modalities

of treatments have failed. The results of tube versus trabeculectomy (TVT) study showed that GDD was found to have a higher success rate and lower reoperation rate at 5 years supporting the use of GDD in the management of complex glaucoma.¹ However, when GDD failure occurs or GDD failed to control the intraocular pressure (IOP) within target levels despite maximal tolerated medical therapy, the next step of

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intervention is still debatable. Revising the GDD, implanting a second GDD, performing a trabeculectomy, or transcleral cyclophotocoagulation (TSCPC) have been used to control IOP in such situation but each was associated with significant risks of complications.

Among these interventions, TSCPC was shown to have less post-operative complications compared to implanting a second GDD.² However, there is paucity of data regarding endoscopic cyclophotocoagulation (ECP) as a second intervention after GDD failure. ECP is a minimally invasive glaucoma surgery (MIGS) that uses laser to produce a controlled and titrable ablation of ciliary process under direct visualisation through an endoscopy developed by Uram in 1992.³ The efficacy and sustainability of ECP in reducing IOP have been widely studied either as single procedure or in combination with cataract surgeries. The results have shown to be promising, as reported by many investigators.^{4,5}

In Malaysia, our center is the only center which is equipped with ECP and serves as the referral center for the whole country. We conducted a study to investigate the efficacy, survival time and safety profile of ECP among our local population.

Methods

A retrospective case series of all patients with previous GDD implantation who underwent ECP from July 2013 to April 2018 were done. All ECP were performed by the same surgeon (JCH) under subtenon anaesthesia. A single clear corneal incision was made with 2.75mm keratome at 11-12 o'clock position. A high molecular weight viscoelastic (Healon GV, Advanced Medical Optics [AMO], Santa Ana, CA) was used to inflate the ciliary sulcus. Diode laser (Iridex OcuLight SL, Mountain View, California, USA) was delivered using the curved endoscopic probe (Endo Optiks, Little Silver, USA)

starting at 150 mW in continuous mode. The ciliary processes and spaces between the processes were treated for at least 270 degrees. The endpoint of treatment was whitening and shrinkage of the processes. Viscoelastic was then removed using either automated or manual irrigation-aspiration (IA). At the end of the procedure, subconjunctival gentamicin 20 mg and dexamethasone 1% 2 mg was injected. All patients received standardised post-operative therapy: guttae ciprofloxacin 0.3% and guttae pred forte 1% every 2 hours tapering dose for 4-6 weeks depending on level of inflammation. Patients were also advised to continue their usual preoperative anti-glaucoma medications.

Data was collected at baseline, 1 month, 3 month, 6 month and 1 year post-operatively. Visual acuity measured with Snellen chart, intraocular pressure (IOP) measured with Goldmann applanation tonometry, number of anti-glaucoma medications and presence of complications were recorded.

Data were recorded in an Excel spreadsheet (Microsoft Office 2007; Microsoft Corporation) and then transferred to SPSS 25 (IBM SPSS Statistics 25, Armonk, NY). The data were analysed for VA, IOP and number of medication used at each time point. Mean IOP and drop use were calculated together with their 95% CIs. Multiple comparisons of VA, IOP and number of anti-glaucoma medications at all-time points were undertaken using repeated measures analysis of variance (ANOVA). Bonferroni's multiple comparison post-test was undertaken to compare pre-treatment IOP with IOP at each subsequent time point. The mean differences in IOP with 95% CIs were given. *p* values <0.05 were considered statistically significant throughout.

Results

Nine ECP cases were performed as a single procedure and one case was a combined

procedure with phacoemulsification. Mean age of the subjects was 39.0 ± 21.0 years old, ranging from 13 to 75 years. There were 5 females and 5 males. Six of them were Chinese, the rest were Malays. The breakdown of the types of glaucoma is shown in Table 1. Seven (70%) of patients had Baerveldt glaucoma implant while three patients (30%) had Ahmed glaucoma implant. None had GDD on both eyes.

All ten eyes from 10 patients were recruited in the study. Eight patients completed six months follow up and subsequently six patients completed one year follow up. The characteristics of patients who underwent ECP are shown in Table 2.

Mean baseline IOP was 17.7 ± 3.74 mmHg. The mean IOP initially went up to 18.1 ± 8.1 mmHg at 1 month but slowly reduced to 18.1 ± 6.1 mmHg, 16.5 ± 5.9 mmHg,

and 15.2 ± 4.8 mmHg at 3, 6 and 12 months respectively. The difference in IOP before and after ECP at all time-points was not statistically significant ($p=0.916$) using repeated measure ANOVA and pairwise comparison between baseline and time points are shown in Table 3.

Mean number of medications at baseline was 4.1 (Table 4). Mean number of medications were reduced at all follow up visits; 2.7, 2.6, 2.5 and 2.5 at 1, 3, 6 and 12 months respectively. The difference in anti-glaucoma medications before and after ECP at all time-points was statistically significant ($p=0.03$) using repeated measure ANOVA and pairwise comparison between baseline and time points are shown in Table 4. However, the mean reduction of number of medications post ECP were statistically significant only up to 6 months.

Table 1: Types of glaucoma in the case series

Types of glaucoma	Number of patients (%)
POAG	2 (20)
JOAG	1 (10)
CACG	1 (1)
Secondary	
Post corneal transplant	1 (10)
Post trauma	1 (10)
Post rhegmatogenous RD	1 (10)
Steroid induced	2 (20)
Necrotising scleritis	1 (10)

POAG: Primary open angle glaucoma; JOAG: Juvenile onset open angle glaucoma; CACG: Chronic angle closure glaucoma; RD: Retinal detachment

Study ID	Baseline			1 Month			3 Months			6 Months			1 Year							
	VA ⁰	IOP ⁰	Meds ⁰	CX ⁰	VA ¹	IOP ¹	Meds ¹	CX ¹	VA ²	IOP ²	Meds ²	CX ²	VA ³	IOP ³	Meds ³	CX ³	VA ⁴	IOP ⁴	Meds ⁴	CX ⁴
1	2.30	16	5	-	2.30	22	4	-	2.30	32	5	RPT	-	-	-	-	-	-	-	-
2	1.30	16	4	-	1.30	12	2	-	1.30	14	2	-	1.30	10	2	-	1.48	7	0	-
3	0.60	17	4	-	0.60	13	1	#	0.60	16	1	-	0.60	12	2	-	0.60	16	4	-
4	0.18	17	4	-	0.18	8	2	-	0.18	16	2	-	0.18	24	3	-	-	-	-	-
5	0.60	26	3	-	0.48	24	3	-	0.60	20	4	-	0.60	20	4	-	-	-	-	-
6	1.78	16	5	-	2.30	24	3	RRD	-	-	-	-	-	-	-	-	-	-	-	-
7	0.48	16	4	-	0.48	20	3	^	0.48	14	3	-	0.60	16	3	-	0.60	14	3	-
8	0.18	23	4	-	0.18	10	2	-	0.48	20	2	-	0.48	22	2	-	0.48	20	4	-
9	0.48	16	4	-	0.60	14	4	-	0.60	20	4	-	0.60	20	4	-	0.60	20	4	-
10	1.80	14	4	-	1.80	34	3	-	1.80	11	0	-	1.8	8	0	-	0.60	14	0	-

*VA, visual acuity; IOP, Intraocular pressure; Meds, number of medications; CX, complications; rpt, repeat; RRD, rhegmatogenous retinal detachment, # hyphaema; ^hypotony

Table 4: Distribution of number of medication at baseline, 1 month, 3 month, 6 month and 1 year post ECP

Time points	Number of patients	Mean + SD and range (mm Hg)	Difference in number of medications compared to baseline [95% CI]**	p value
Baseline	10	4.1 + 0.6 3.0 - 5.0	-	
1 month	10	2.7 + 0.9 1.0 - 4.0	-1.40 + 0.97 (-2.01 to -0.71)	0.001
3 month	9	2.6 + 1.6 0 - 5.0	-1.44 + 1.59 (-2.67 to -0.22)	0.026
6 month	8	2.5 + 1.3 (0 - 4.0)	-1.38 + 1.50 (-2.63 to -0.12)	0.036
1 year	6	2.5 + 2.0 (0 - 4.0)	-1.50 + 1.98 (-3.57,0.57)	0.122

*ECP: endoscopic cyclophotocoagulation

The visual acuity at baseline, 1-month, 3-month, 6-month and 1 year post ECP were shown in Table 1. Analysis of visual acuity showed that 3 patients had decrease of Snellen vision of 1 line (1 was due to worsening of corneal decompensation, 2 were due to ocular surface problems) and 1 had decrease of 2 lines of vision (due to cataract progression).

The complications post ECP were minimal (Table 2). Transient self-limiting hyphaema was seen in one patient. Another patient developed hypotony with choroidal effusion on day 1 post-operative but hypotony resolved within 1 week. Uncontrolled IOP was seen in one patient post ECP and was subjected to another ECP five months after the first ECP. Another patient needed surgery for recurrent rhegmatogenous retinal detachment (RRD) two months after ECP procedure. No excessive anterior chamber inflammation or other complications were reported.

Discussion

Management following primary GDD failure remains a challenge. TSCPC has been one of the successful methods used but it is

a blind treatment without direct visualisation of the ciliary bodies. With the invention of ECP, precise and accurate ablation of ciliary body is possible to reduce the aqueous outflow, thus, reducing the IOP with comparative minimal complications. Our study showed that ECP was able to reduce the IOP and number of anti-glaucoma medications post procedure with mild and transient complications.

Studies have shown the potential of ECP in controlling IOP, either in combination with cataract surgery or as rescue procedure after failed initial glaucoma surgery, with relatively low risk of complications.⁶ Francis et al reported a success rate of 88% using ECP in the management of failed prior tube shunt from 6 months up to 2-year follow up with no serious complications. Both mean IOP and number of medications were reduced significantly post ECP.⁶ While, a review by Murakami et al found that both ECP and implantation of a second GDD were equally effective in lowering IOP ($p=0.52$) and number of anti-glaucoma medications ($p=0.50$) at 2 years follow up for patients with refractive glaucoma that has failed a prior GDD.⁷

ECP was also compared to Ahmed valve in the management of patients with failed trabeculectomy, with the IOP of > 35mmHg. The study showed that the success rate at two years for both groups were similar, 71% for the Ahmed group and 74% with ECP.⁸

Although the IOP reduction post ECP in our study was not statistically significant, the number of medications were significantly reduced up to 6 months. The differences in these findings compared to other studies might be attributed to the fact that, at baseline, our patients were on higher number of medications leading to a lower mean IOP. In cases where patients were on systemic anti-glaucoma agents, we managed to discontinue the systemic anti-glaucoma agents with an acceptable IOP post ECP.

However, this is a retrospective study and subject to non-response and recall bias. Some patients were followed up and managed by the referring hospital after ECP. Thus, there was lack of standardisation in terms of post-op management. The treatment of ciliary processes was only 270 degrees in our study compared to some studies where more aggressive approach of treating more than 270 degrees¹⁰ or near to 360 degrees⁶ were applied. This needs to be studied to determine its additional benefits compared to the risks of complications such as hypotony and pthisis bulbi.

In view of minimally invasive nature of ECP, less complicated post-op care and good safety profile, ECP offers an alternative in managing failed primary GDD in glaucoma patients if facilities are available. A prospective study with a bigger sample size and longer follow up period may offer a better assessment of efficacy and safety profile of ECP in our population.

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Clinical characteristics and surgical outcome of eyelid ptosis at tertiary eye hospital: a retrospective study

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Background: Ptosis is a common upper eyelid problem which can be seen in children and adult. Ptosis can cause amblyopia in younger patients and reduce visual field in older patients.

Objectives: To determine the prevalence and clinical characteristic of ptosis and to evaluate surgical outcome of eyelid ptosis.

Methods: In this descriptive-retrospective study, 490 medical records of patients who admitted to Jakarta Eye Center Hospital between 2014 and 2016 with diagnosis of eyelid ptosis were included in this study. Prevalence rates, patient's demographic, clinical characteristic, type of therapy, successful rate and complication of ptosis surgery were evaluated.

Results: The prevalence of ptosis in this study was 490 patients and was more frequent in men aged 44.5 years old. The ptosis was predominantly unilateral 79.6%. Ptosis was mild in 33.5% cases and myogenic ptosis was the most common etiology of ptosis in this study. Levator resection is the most prevalent type of surgery. The success rate of ptosis surgery was 91.8%.

Conclusion: The success rate of ptosis surgery in this study was high and undercorrection was the most common complication of ptosis surgery.

Conflict of Interest: There is no conflicting relationship exists for any author.

Keywords: eyelid ptosis, levator resection, successful rate, ptosis surgery.

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Introduction

Ptosis or blepharoptosis is a dropping of the upper eyelid that can occur unilaterally or bilaterally.¹ Ptosis is one of the most common upper eyelid abnormalities in oculoplastic practice that affects visual field and could reduce visual acuity. Ptosis can be present as mild to severe condition.² Ptosis can be classified as congenital and acquired and has variety of etiology such

as myogenic, neurogenic, traumatic, mechanic, neuromuscular, neurotoxic, involutional or aponeurotic, and pseudoptosis.² Study by Baiyeroju et al³ stated there were 25 cases of ptosis during 5-year period, 52% of the patients were found to be less than 16 years of age while 8% were over 50 years of age.³ The sex ratio of ptosis between men and women was quite similar 1:1 and 68% cases was unilateral.⁴

Comprehensive eye examinations consist of history taking, physical and ophthalmological examination are important to make the diagnosis and to determine the treatment. It is also important to perform the specific

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eyelid measurements such as margin reflex distance (MRD), margin limbal distance (MLD), vertical palpebral fissure (VPF), levator action (LA), bell's phenomenon, lid lag, and skin crease in ptosis cases. Photograph before and after therapy should also be taken in order to assess the improvement after therapy.⁴

Management of ptosis depends on the underlying etiology. Not all ptosis cases should be performed surgery. Surgical management could be performed in congenital, involutional, or mechanical ptosis which obstructs the visual field and visual acuity. The purpose of this study is to determine the prevalence rate, demographic and clinical characteristic of ptosis patients, type of therapy, and the success rate of ptosis surgery in Jakarta Eye Center Hospital, Indonesia.

Methods

This is a descriptive-retrospective study. Medical records of 490 patients who first diagnosed with eyelid ptosis between January 1st 2014 and December 31st 2016 in Jakarta Eye Center Hospital were analyzed. The success rate of ptosis surgery was assessed based on the presence of ptosis after surgery, the equal point or at least

1 mm difference of Margin Reflex Distance (MRD) and Vertical palpebral fissure (VPF) before and after surgery for unilateral ptosis and the equal point of MRD and VPF after surgery with MRD and VPF in normal patient for bilateral ptosis and the presence and absence of complication of surgery. The choice of surgical type procedure for ptosis repair in this study depends on the degree of levator function. If the levator function is poor ($LA < 4$ mm), frontalis suspension with fascia lata approach will be performed. If the levator function is moderate until good ($LA 4-12$ mm), levator resection approach will be performed. If the levator function is excellence ($LA > 12$ mm), levator advancement approach will be performed. Data analysis was performed on all variables.

Results

In this study, the number of ptosis patients was quite similar between male (54%) and female (46%) with ratio $\pm 1.2:1$. From the demographic data as shown in table 1, unilateral ptosis is more predominant compared with bilateral. The median age of ptosis is 44.5 years old with the minimum age 2 weeks and maximum age 94 years old.

Table 1: Demographic characteristic of ptosis patient in JEC hospital in 2014 – 2016

Demographic	Number of patients (n=490)	Percentage (%)
Gender		
Male	266	54.3
Female	224	45.7
Laterality		
Unilateral	390	79.6
Bilateral	100	20.4
Age (years)		Median (min –max)
		44.5 (1-94)
1-19	206	42
20-39	89	18.2
40-59	117	23.9
≥ 60	78	15.9

Figure 1: shows a significant increase in the number of ptosis patient in 2015 by 40%. While in the year 2016 there were also an increase for only 7%.

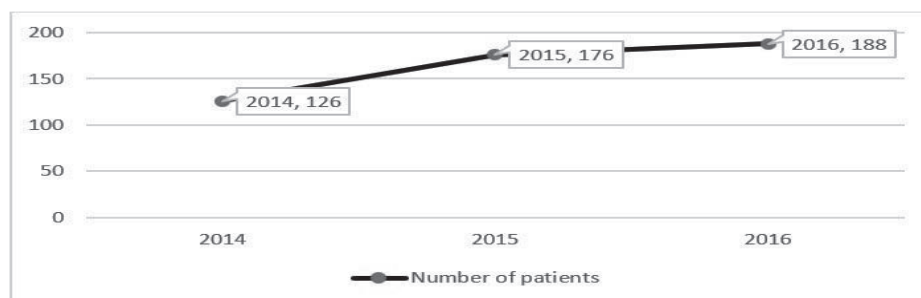


Table 2 shows that most of the patients had acquired ptosis (73.7%) while the others had congenital ptosis (26.3%). Mild ptosis was more often in this study compared to moderate and severe ptosis. The most common etiology of ptosis was myogenic (33.1%) and involutional ptosis (24.7%).

Table 2: Clinical characteristic of ptosis patients in JEC hospital in 2014-2016

Clinical characteristic	Number of patients (n=490)	Percentage (%)
Type of ptosis		
Congenital	129	26.3
Acquired	361	73.7
Degree of ptosis		
Mild	164	33.5
Moderate	135	27.6
Severe	113	23.1
N/A	78	15.9
Etiology of ptosis		
Myogenic	162	33.1
Involutional	121	24.7
Neurogenic	111	22.7
Traumatic	78	15.9
Mechanic	3	0.6
Pseudoptosis	15	3.1

Most of the patients had been planned to have surgery (46%), while 27.7% was observed and others were still required further examination such as orbital CT-Scan, head MRI or EMG and in need of consultation to another department and division to figure out the etiology of ptosis as shown in table 3.

In surgical management, which is shown in figure 2, 160 patients were planned to perform levator resection surgery, 55 patients frontalis suspension with fascia lata graft surgery, and

1 patient levator advancement surgery; only 122 patients were performed ptosis surgery as shown in table 4. We included preoperative and postoperative condition of 2 patients in Figure 3. The success rate of ptosis surgery was 91.8% and only 8.2% required second ptosis surgery. The surgeries were done by 3 surgeons who are equally competent in this field and the surgery outcomes were not significantly different. The most frequent complication of surgery in this study was undercorrection (4.9%) as shown in table 5.

Table 3: Type of ptosis therapy at JEC eye hospital in 2014-2016 (n = 490)

Management	Number of patients (n=490)	Percentage (%)
Surgery	225	46
Observation	136	27.7
Medicine	45	9.2
Ancillary test	37	7.5
Further consultation	47	9.6

Figure 2: Surgical management plan of ptosis patient at JEC eye hospital in 2014-2016 (n = 225)

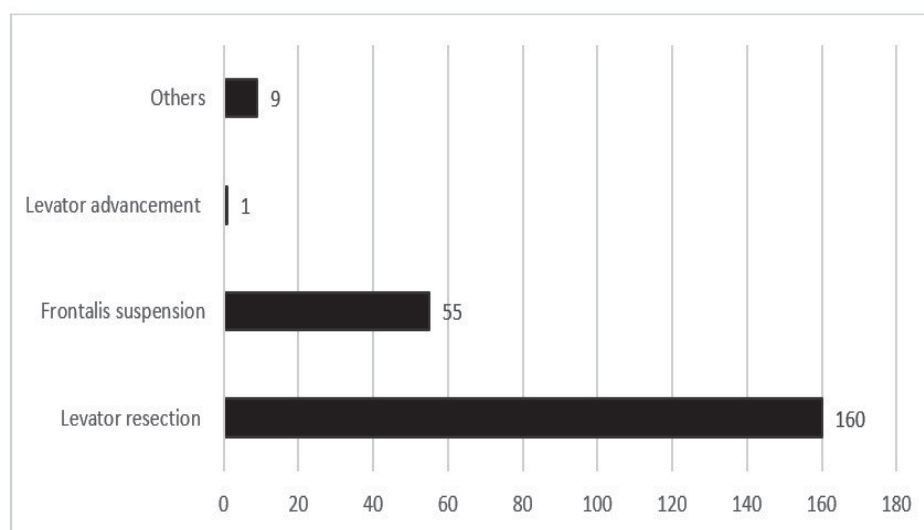


Table 4: Evaluation of ptosis surgery at JEC eye hospital in 2014-2016 (n=122)

Surgery Result	Number of patients (n=122)	Rate (%)
Success	112	91.8
Failure	10	8.2

Figure 3: a. Ptosis with good levator action preoperative condition; b. Post levator resection surgery; c. Ptosis with poor levator action preoperative condition; d. Post frontalis suspension surgery

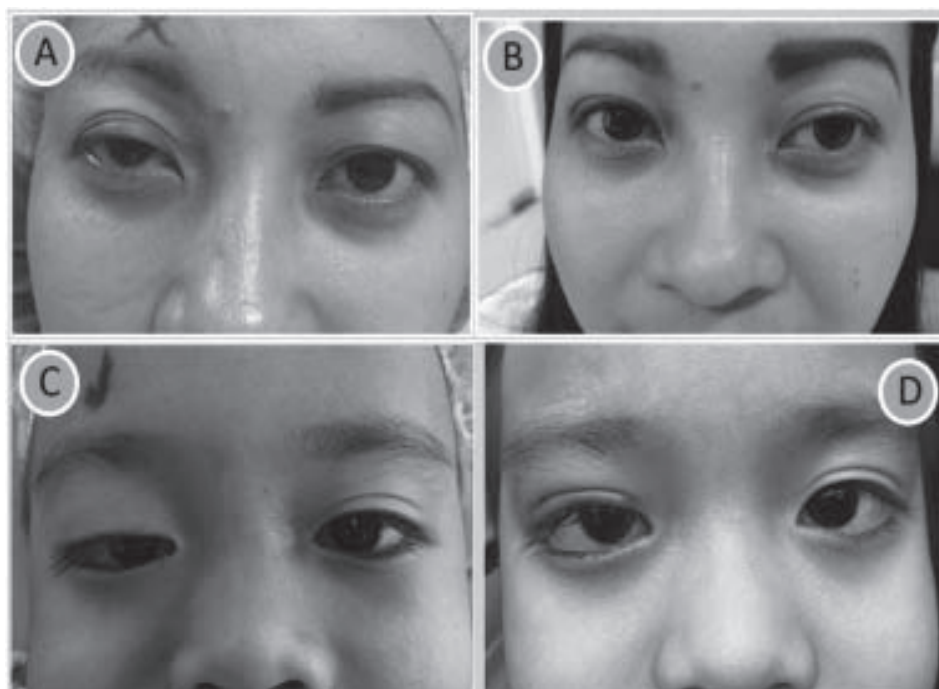


Table 5: Complication after ptosis surgery at JEC eye hospital in 2014-2016 (n=10)

Complications	Number of patients (n=10)	Percentage (%)
Undercorrection	6	4.9 %
Overcorrection	2	1.6 %
Palpebral cicatrix	1	0.8 %
Excessive skin	1	0.8 %

Discussion

Ptosis is one of the most common abnormalities of the upper eyelid. In this current study, the prevalence of ptosis at JEC eye hospital between 2014 and 2016 was 490 cases. In 2014 there were 126 cases of ptosis and there was a significant increase in 2015 by 40% to 176 cases of ptosis and slightly increase by 7% to 176 cases in 2016. In contrast to our study, Balasubrahmanian K et al⁵ showed the incidence of

ptosis in tertiary hospital in Thanjavur India was only 109 cases.

In this study 54.3% were male and 45.7% were female with male to female ration of 1.2:1 as shown in table 1 which is comparable with the observation of Balasubrahmanian K et al⁵ of 61.5% males and 38.5% females. Skaat et al⁶ also showed a male predominance in the study of 56.7%. Some literature stated that gender is not an associated factor for ptosis. The weakness

or dysgenesis of levator muscle, the presence of history of eye surgery or upper eyelid trauma, the weakness of the 3rd nerve, the presence of upper eyelid tumor are the main predisposing factors for ptosis.¹

In our study, unilateral ptosis was more predominant by 79.6% compared to bilateral ptosis by 20.4%. Abrishami et al⁷ reported the similar result in their series at tertiary hospital in Iran by 90.5% of unilateral ptosis. The median age of patients in our studied population was 44.5 years with the age range from 1-94 years which is consistent with study of Hashemi et al⁸ who observed the age range to be from 1-96 years in Tehran population. In our study, most of the ptosis patients were at age range 1-19 years by 42%. Hashemi et al⁸ stated the similar result of the ptosis patient came at age range 1-19 years by 37.5%.

In our series, acquired ptosis was the most common type of ptosis (74%) compared to congenital ptosis (24%). Clinically, most of the ptosis patient who came to our hospital had mild ptosis. In contrast with Balasubrahmanian et al⁵ in their series showed the majority of patients who came in Thanjavur India were moderate ptosis by 61.54%. In this current study the most common etiology of ptosis were myogenic (33.1%), followed by involutional/aponeurotic (24.7%), neurogenic (22.7%), traumatic (15.9%), pseudoptosis (3.1%) and mechanical (0.6%). In contrast with retrospective study by Gonzalez et al⁹ showed the most common etiology were involutional (52.9%), followed by congenital (27.1%), mechanic (8.9%), myogenic (3%), neurogenic (4.6%), and traumatic (3.3%).

Not all ptosis cases are performed surgery. Surgical management can be performed in congenital, involutional/aponeurotic and mechanical ptosis. In our study, 46% patients were planned to have surgery, 27.7% was observed, 9.2% got some

medicine, 7.9% still needed further examination such as orbital CT-Scan, head MRI, and EMG, the last 9.6% still needed consultation to another department/division. Of 46% patient who planned to have a surgery, only half underwent the surgery. Types of surgical management at JEC eye hospital between 2014 and 2016 were 160 cases levator resection, 55 cases frontalis suspension with fascia lata, 1 case levator advancement and others were performed tumor excision and reconstruction of fracture. The result of ptosis surgery in this series was determined by the presence of ptosis after surgery, comparison MRD and FPV before and after surgery and the presence of complications after surgery. The successful criteria are the absence of ptosis after surgery, an equal or at least 1 mm difference of MRD and FPV before and after surgery, and the absence of complication after surgery.

In this current study of 122 patients who had been performed surgery, the success rate of ptosis surgery was 91.8% and only 8.2% was failed and needed a second surgery. Our study has a higher result compared to the study by Abrishami et al⁷ and Jordan et al¹⁰ which showed the success rate of levator resection surgery was 78.7% and 43%, respectively.

In our study, the most common complication was undercorrection by 4.9% which are similar to the study of Abrishami et al⁷ and Tyers et al¹¹ in their studies that stated undercorrection was the most common complication (19.1% and 19%). Levator resection was the type of surgery that caused all cases of undercorrection in this study. The surgeon did resurgery to make sure that the complication was well-managed. Other potential complications in ptosis surgery include overcorrection, unsatisfactory or asymmetric eyelid contour, scarring, wound dehiscence, eyelid crease asymmetry, conjunctival prolapse, and lagophthalmos with exposure keratitis.⁵

In this study, other complications were overcorrection (1.6%), palpebral cicatrix (0.8%) and excessive skin (0.8%).

Our study was retrospective which took secondary data from medical record, hence some data that we required were incomplete. Therefore, we need further prospective study.

Conclusion

The prevalence of ptosis at Jakarta Eye Center eye hospital between 2014 and 2016 was 490 patients. Ptosis was higher in men in the age of 44.5 years old and was predominantly unilateral. The success rate of ptosis surgery was high and the most common complication was undercorrection.

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Outcome of needle revisions with subconjunctival 5-fluorouracil in filtration blebs

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Objective: To study the outcome of subconjunctival needling with 5-fluorouracil in filtration blebs in the patients who have been treated by trabeculectomy.

Methods: Retrospective chart review of glaucoma patients who have been treated by trabeculectomy or combined phaco-trabeculectomy, and needling revision in accordance to indications at Thammasat University Hospital from January 2015 to December 2017 in total of 52 eyes. The treatment result was monitored during a 6 month- period. Success outcome by monitoring IOP and factors affecting failure of procedure are outcome measurement. In needling procedure, 27-gauge needle and 0.1 mL of 50 mg/mL of 5-FU were used.

Results: After needle revision, mean IOP decreased from 20.5 ± 6.77 mmHg to 13.35 ± 8.11 mmHg at 6 months ($p < 0.001$), median IOP reduction was 29.70%. Complete success, qualified success and failure were at 63.46%, 19.23%, 17.31%, respectively. Incidence rate of failure was 7.92, using Kaplan-Meier survival analysis. Risk factors for failure of 5-FU needling were pre-needling IOP ≥ 25 mmHg (HR 3.81, $p = 0.047$) and secondary glaucoma including NVG (HR=2.6, $p = 0.154$). In addition, serious complication was not detected after monitoring of treatment for 6 full months.

Conclusion: Bleb needle revision could reduce IOP in the patients who failed filtering bleb and could restore function of bleb in the patients with increasing trends in IOP from bleb morphology which is at safe and effective procedure.

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

Keywords: glaucoma, trabeculectomy

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Introduction

The current treatment of glaucoma consists of topical eye drops, laser and surgery. Trabeculectomy is a surgical treatment of choice in various glaucoma patients. Trabeculectomy is a treatment to reduce

intraocular pressure by shunting aqueous from the anterior chamber to subconjunctival space. The surgical indications include inability to control intraocular pressure and existence of worsening illness despite various combinations of antiglaucoma medications or adherence issues due to complications from eye drops, etc. Success rate of this type of surgery is high. However, findings indicated that success of surgery annually decreased around 10%. Affecting factors contributing to trabeculectomy failure include scarring or fibrosis

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between conjunctiva and episclera layer, resulting in intrableb fibrosis, decrease in aqueous drainage, and inability to control intraocular pressure in the main phase. Various methods that contribute to the effectiveness of a bleb and modulation of wound healing processes to reduce fibrosis includes bleb massage, laser suture lysis, and use of adjunctive antifibrotic agents such as mitomycin C and 5-fluorouracil during surgery or after surgery. Transconjunctival needling revision is used to remove part of fibroses with minimally invasive technique and to restore infiltration. The indications of needle revision consist of bleb encapsulation, inadequate IOP control with an elevated bleb with microcysts, flat bleb with visible sclera flap without microcyst, or any of the aforementioned requiring a topical ocular hypotensive medication, dysesthetic blebs, and leaking blebs. Chart review-based study was conducted to report the outcome of needle revision at 6 months after the procedure. The factors affecting needle revision failure were studied, safety and contingent complications after the procedure were reported. The study was conducted by reviewing charts patients who underwent trabeculectomy and have been treated with needle revision which their intraocular pressures could not be controlled after surgery or other aforesaid indications were existent.

Methods

Retrospective chart review is conducted on patients at Thammasart University Hospital for a total of 52 eyes. The patients underwent trabeculectomy or a combination of phaco-trabeculectomy or second trabeculectomy. After surgery, needling with 5-FU was performed in accordance with the following indications including inadequate IOP control ≥ 21 mmHg with an elevated bleb with microcysts, trend to increase IOP from bleb morphology, leaking bleb, dysesthetic blebs⁹ and patients have been excluded in case of

incomplete data of medical records. Treatment results after needling with 5-FU is monitored until 6 months. Data from medical records were collected from January 2015 to December 2017.

Statistical Analysis

Qualitative variables are reported in percentage and continuous variables are reported in mean \pm SD and median. Cox hazards regression is applied for analyzing each factor to whether it affects failure. Wilcoxon signed-rank test is conducted to compare IOP, number of medications and visual acuity before and after procedure, and Mixed model and pair t-test are conducted to compare IOP of each visit. In addition, Kaplan-Meier survival analysis for failure is applied.

Bleb needle revision technique

In topical anesthetic, 0.5%Tetracaine Hydrochloride is used at least 4-5 times every 5-10 minutes in combination with vasoconstrictor (Phenylephrine 2.5%). Eye drops are instilled before the procedure. All bleb revisions were performed under slit lamp in a medical examination room.

A 27 guage needle was connected to an syringe insulin. Syringe filled with 5-fluorouracil at a concentration of 50 mg/ml with a volume of 0.2 ml. Eye speculums were used to open the patient's eyes. The needle was inserted into the site of subconjunctiva around 10 mm away temporally or nasally to the site of sclera flap and then straight to main loculation where is over to the site of sclera flap. The needle tip is beveled up and is used to cut and open any episcleral fibrosis. In cases of minimal effect, slides may be performed below the scleral flap to lift the scleral flap or enter the anterior chamber through the filtering ostomy. Restoration of aqueous drainage is considered to be the end point. Vessels, and perforation of any conjunctiva is avoided and no suturing conjunctival is required after the injection of 5-fluorouracil

(50mg/ml) for 0.1 ml into subconjunctiva by injecting over and at the back to the site of blebs.

Leaking point or bleeding after procedure is checked. Eye speculum is removed then topical antibiotic is instilled. The patients are instilled with topical steroid (Prednisolone 1%) every 2 hours and topical antibiotic every 4 hours by day, and they are continuously instilled at home after returning home.

Data Collection

Data was collected from review chart of outpatients by collecting demographic data such as age, gender, type of glaucoma, type of operation trabeculectomy, second trabeculectomy or combined phaco-trabeculectomy, period after trabeculectomy to first needling, number of antiglaucoma medications, IOP, total number of times of needling, total volumes of 5-FU, and visual acuity. Data at 1 week, 1 month, 3 months and 6 months after needling procedure was collected.

Outcome measurement

Success outcome of needling with 5-FU at 6 months period and report of factors affecting failure are defined as the following. Complete success was defined as intraocular pressure (IOP) below 21 mmHg without antiglaucoma medication and reduction of intraocular pressure more than 20 % from beginning intraocular pressure without combination of antiglaucoma medication. Qualified success is defined as intraocular pressure below 21 mmHg in combination with antiglaucoma medication and reduction of intraocular pressure more than 20 % from beginning intraocular pressure in combination with antiglaucoma medication.

Failure is defined as intraocular pressure of more than or equaling to 21 mmHg or reduction of intraocular pressure lesser than 20% from beginning intraocular pressure or poor vision equaling to no light percep-

tion or operative requirement for reduction of intraocular pressure such as glaucoma drainage devices, cyclophotocoagulation, cryotherapy, etc.

Results

According to chart review, we found underwent filtering surgery and needle revision with adjunctive 5-FU for a total of 52 eyes, consisted of 32 men (61.54%) and 20 women (38.46%). Mean age \pm SD was 62.01 \pm 10.18 (range, 37 to 87). Patient demography is shown in Table 1.

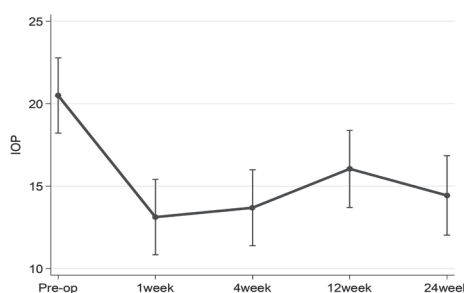
Types of preneedling operations included the patients who were underwent trabeculectomies for 32 eyes (61.54%), trabeculectomies in combination with cataract surgery for 19 eyes (36.54%) and second trabeculectomy for 1 eye (1.92%). All patients in research were administered with 0.4 mg/mL of MMC during their original surgery to be soaked onto cellulose surgical sponge with an application duration ranged between 150 and 180 seconds.

The median interval between original filtration and first needling procedure was 64.5 days, with a range of 3 days to 6 years. Mean total number of needle revisions was 2.61 \pm 2.48 times and median was 2 times (range, 1 to 13).

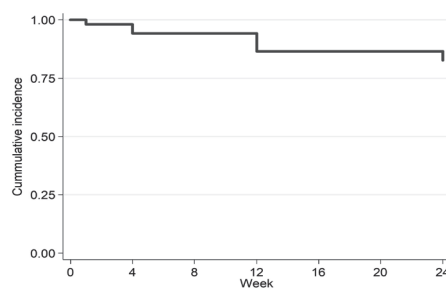
The finding indicated overall mean IOP reduction at 6 months was 27.68 \pm 25.44%, median was 29.70% with range of 0 to 70%. Mean preneedling IOP was 20.5 \pm 6.77 mmHg, mean postneedling IOP at 1 week, 1 month, 3 months and 6 months were 13.11 \pm 8.71, 13.49 \pm 7.56, 15.44 \pm 10.24, and 13.35 \pm 8.11 mmHg, respectively. IOP values statistically significantly decreased in every postneedling visit ($p<0.001$). The change in IOP is illustrated in Figure 1. Complete success for 33 eyes from 52 eyes on criteria basis was 63.46%. Mean \pm SD preneedling IOP was 19.30 \pm 7.13 mmHg, decreasing to be 11.33 \pm 3.14 mmHg at the 6th month ($p<0.001$). Postneedling IOP statistically significantly decreased in

Table 1: Patient demography

Demographic Factor	N	Percent
Total number of patients	52(eyes)	100
Gender		
Male	32	61.54
Female	20	38.46
Eye		
Right	33	63.46
Left	19	36.54
Diagnosis		
POAG	19	36.54
PACG	16	30.77
NVG	9	17.31
Secondary Glaucoma	8	15.38
Initial Surgery		
Trabeculectomy	32	61.54
Combined phaco-trabeculectomy	19	36.54
Second Trabeculectomy	1	1.92
Indication of needle revision		
IOP > 21 mmHg	28	53.85
Bleb morphology	22	42.31
Bleb leakage	2	3.85

**Figure 1:** The change in IOP

every visit upon comparison with preneedling. Qualified success for 10 eyes from 52 eyes was 19.23%. Mean preneedling IOP was 20.90 ± 5.44 mmHg, decreasing to be 14.50 ± 4.50 mmHg ($p=0.032$). IOP values also statistically significantly decreased upon comparison with preneedling IOP. Failure of 9 eyes was 17.31%. Mean IOP was 21.0 ± 1.41 mmHg. Post-needling IOP did not decrease. The finding indicated mean at 41.0 ± 26.87 mmHg,

**Figure 2:** Incidence rate of failure at 7.92 using Kaplan-Meier survival analysis

median at 41 mmHg, with range of 22 to 60 mmHg. Incidence rate of failure at 7.92 using Kaplan-Meier survival analysis as shown in Figure 2. According to 9 eyes in the group of failure, 8 eyes of patients were further operated by glaucoma drainage device, and the other 1 eye of patient was treated with cryocyclotherapy. Potential risk factors for failure are shown in Table 2. There was no significant differ-

Table 2: Hazard ratio failure of bleb needling

Study Factors	Category	Hazard Ratio	95%Confidence Interval	P-Value
Gender	Male	1.26	(0.31,5.04)	0.743
	Female	1		
Eye	Right	1	(0.61,8.59)	0.213
	Left	2.3		
Diagnosis	Primary Glaucoma	1	(0.69,9.68)	0.154
	Secondary Glaucoma	2.60		
Preneedling IOP	High (≥ 25 mmHg)	3.81	(1.02,14.23)	0.047
	Low (< 25 mmHg)	1		

ence with respect to gender or laterality. Upon comparison between primary glaucoma including POAG and PACG, and secondary glaucoma including NVG, the finding revealed that secondary glaucoma including NVG was rather the risk factor of the group of failure at hazard ratio of 2.60 ($p=0.154$). There was indifference with respect to time to needling in the group of success upon comparison with the group of failure ($p=0.72$) using Wilcoxon rank-sum test method. The finding revealed that preneedling IOP particularly when $IOP \geq 25$ mmHg affected failure rather than in the group where IOP was lesser than hazard ratio at 3.81 ($p=0.047$). Mean number of preneedling antiglaucoma medications was 0.32 ± 0.73 and median was 0 (range 0-3); and mean number of postneedling antiglaucoma medications was 0.56 ± 1.09 and median was 0 (range 0-4). The finding indicated that there was indifference of number of drugs before and after operation whereas p value was 0.11, no serious complication, no visual loss up to no light perception in studying group and no decrease in visual acuity by 2 or more snellen line. Preneedling mean \pm SD logMAR VA was 0.76 ± 0.86 and median was 0.54, with a range of logMAR 0 to logMAR 3. Postneedling mean \pm SD logMAR VA was 0.85 ± 1.02 and median was 0.50, with a range of logMAR 0 to logMAR 3. There was statistical significant indiffer-

ence whereas p value was 0.88. Postneedling leakage was detected for 1 case from total number of cases and conservative treatment was performed.

Discussion

The significant cause of trabeculectomy bleb failure was scarring and fibrosis at episclera. Various treatment methods included from antiglaucoma medication to re-surgery. Needle revision is the simple and effective operation in rescuing bleb. Revision of failed filtration bleb through a small conjunctival incision was first described in 1941. After that, many authors have proposed various methods from use of needle gauges in different no. to small needle knife but under the same principle of disrupting subconjunctival scar tissue and restoring bleb function.^{1,2} Several studies have used either 5-fluorouracil (5-FU) or mitomycin-C (MMC) in needling. 5-FU has been more preferred for use by most of around over 60%. Wei Liu et al.⁶ studied comparative case series in comparison between subconjunctival MMC (0.1 mL of 0.2 mg/mL) and 5-FU (0.1mL of 50 mg/mL) in needling. The finding indicated that MMC was more effective than 5-FU for early dysfunction bleb. Meanwhile, Palejwala et al.⁸ found that there was no apparent difference between the use of 5-FU and use of MMC. In our research, adjunctive subconjunctival 5-FU was used

in combination with needling for all cases in concentration of 0.1 mL of 50 mg/mL. After monitoring treatment until completing 6 months, serious complication from injection of subconjunctival 5-FU was not detected.

Regarding to outcome, several studies reported success rate of needling ranging from 39% to 91%, depending on criteria in each study and studying duration.³ In our research, complete success, qualified success and failure are defined in similarity to several researches. David C. Broadway et al.³ reported the outcome of needle revision in combination with subconjunctival injection using 5-fluorouracil in the patients who were used to be performed for surgery in shunting aqueous from eyeball to subconjunctival space and intraocular pressure was uncontrollable after surgery. The monitoring was performed at least 9 months after surgery for 101 eyes. The definition of success outcome is 1 reduction of intraocular pressure lesser than 22 mmHg, or 2. reduction of intraocular pressure more than 30% from the beginning intraocular pressure. The finding indicated success rate at 75% in 1 year, 52% in 3 years, and 56% in 1 year, 40% in 3 years in accordance with definition 1 and 2, respectively. Mustafa S. Kapasi et al.⁵ studied the efficiency of subconjunctival needling revision using 5-FU when administered to patients who had non filtering, flat, or encapsulated blebs over 1 year after the original surgery, under 2 years period of treatment outcome monitoring. The finding of the studying result revealed that mean intraocular pressure decreased from 23.5 mmHg to be 13 mmHg (10.5 mmHg at 44.8%). It was concluded that late 5-FU needling was an effective method to control IOP. Yung-Sung Lee et al.⁷ studied risk factor of failure of needle revision in combination with subconjunctival injection using 5-fluorouracil in the patients who failed from surgery in shunting aqueous

from eyeball to subconjunctival space for 41 eyes. The definition of success is intraocular pressure lesser than 21 mmHg or reduction of beginning intraocular pressure at least 20% without drug combinations. The finding revealed that survival of blebs at 6, 12 and 24 months were 42%, 39% and 23%, respectively. In our research, the finding indicated decrease in mean IOP from 20.5 ± 6.77 mmHg to be 13.35 ± 8.11 mmHg, mean percentage of IOP reduction was 27.69%, and success rate consisting of complete and qualified success was 82.69%. Upon analysis on statistical data, the finding revealed statistical significant decrease in IOP upon comparison with beginning IOP in every visit at week 1, month 1, month 3 and month 6 both in the groups of complete success and qualified success. However, due to 22 eyes from 52 eyes (42.31%) that were treated with needling in accordance with bleb morphology indication, there was a tendency of failure, whereas beginning IOP was not higher than 21 mmHg, this indication maybe over indicated. As a result this study found no statistical difference of number of medications before and after procedure that was dissimilar to several previous paper. Several researches reported that bleb morphology affected postneedling bleb survival.⁷ The finding revealed that small central bleb extension and flat bleb were higher related to the opportunity of failure.² In this research, this variable was not studied since it is retrospective study. Grading system data result was differently recorded by each surgeon and bleb morphology data was incomplete. Therefore, the said data was not taken for analysis. However, the finding indicated that bleb morphology in the group of failure was often in flat bleb and thick tenon.

In this research, the finding revealed failure due to IOP > 21 mmHg and surgical requirement for other operations for 9 eyes from total of 52 eyes or 17.31% and

incidence rate of failure around 8%. Several researches studied factors affecting preneedling bleb survival and the finding indicated that there were similar risk factors such as preneedling IOP > 30 mmHg, no use of mitomycin C during trabeculectomy, immediate IOP after needle revision > 10 mmHg, time to first needling < 4 months, high IOP after needle revision within 1 week, and bleb morphology as aforementioned. The author's finding of this research revealed that the statistical significant affecting factor included preneedling IOP \geq 25 mmHg (HR 3.81, $p=0.047$). Other factor that might have clinical effect but had no statistical significance included type of glaucoma particularly in the group of secondary glaucoma such as NVG and uveitic glaucoma that risk of failure was detected at bleb rather than the group of primary glaucoma (HR 2.60, $p=0.154$). There was statistical significant indifference on gender, laterality, and time to first needling. Due to recording of incomplete data in medical records, postneedling immediate IOP was not taken for statistical analysis.

Regarding to safety after monitoring until completing 6 months, serious complication such as loss of vision up to no light perception was not detected. The finding indicated that log MAR VA value was indifferent before and after procedure. Just one case was detected for leakage after needling and recovered by conservative treatment. The report of infection or hypotony was not detected at all.

Limitation of this research included retrospective chart review, resulting incompleteness and inadequacy of some data taken for analysis such as immediate IOP reduction, bleb morphology, etc. Even though needle revision was operated using the same technique but there might be variables from surgeons due to the operations by various surgeons. In addition, 6 months treatment monitoring period might be too

short, resulting in insufficient examination of long-term perspective. Possible future directions will include prospective study for eliminating variables that may affect research, recording and collecting data necessary for research, and scheduling longer monitoring period.

Conclusively, needle revision was useful for patients who were unable to control IOP after trabeculectomy in term of restoration of IOP control to be within the criteria throughout 6 months monitoring period, ability to restore function of bleb, easy and safe procedure. The risk factors affecting failure included secondary glaucoma especially NVG and preneedling IOP which was more than 25 mmHg.

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Comparison of mydriatic effect and irritative symptoms between mydriatic drug-soaked sponge packing and conventional instillation

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Objective: To evaluate the pupil diameter and irritative symptom by the using of mydriatic drug-soaked sponge packing versus conventional instillation technique in the patients who need fundus examination.

Methods: With 40 patients, were dilated pupils by applying mydriatic drug-soaked sponge in one eye and using conventional technique in another eye. The soaked sponge were packed for 20 mins, pupils' diameter was checked every 10 mins for 3 times, and recorded irritative symptom in 30 mins.

Results: The mean pupil diameter after mydriatic drugs applying at 10, 20 and 30 minutes were 3.2 ± 1.0 , 5.5 ± 1.3 and 7.0 ± 1.1 mm. by drug soaked sponge technique versus 3.2 ± 0.8 , 5.4 ± 1.1 and 6.5 ± 1.0 mm by conventional technique respectively ($p=0.661$, 0.682 , 0.974). The irritative symptom score was 4.9 ± 2.6 in mydriatic drug soaked sponge group and 3.0 ± 2.4 in conventional group ($p=0.0006$).

Conclusion: The mydriatic drug soaked sponge technique can provide a similar mydriatic effect to the conventional instillation technique. The sponge technique uses less number of staff and their effort. However this technique can cause significant irritation or foreign body sensation in some patients.

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

Keywords: mydriatic, cataract, intraocular pressure, soaked-sponge technique

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Introduction

In general, the influence of light on human eyes affects pupil reaction; pupil diameter will constrict to approximately 2-3 mm after exposure to light. Patients who require fundus examinations or cataract surgery should have dilated pupil diameters up to approximately 7mm.^{1,2} Currently, the general method of pupil dilation consists of 2 types of topical eye drops; 1%Tropicamide

and 10% Phenylephrine. The majority of methods for the conventional technique is by instilling 1% Tropicamide and 10% Phenylephrine into the lower conjunctival fornix; or alternately, by instilling every 5 minutes until 30 minutes^{3,4}, until the pupil diameter is dilated to 7-9 mm. The possible side effects of 1%Tropicamide eye drops are high intraocular pressure, dry mouth, blurred vision, sensitivity to light, tachycardia and headache. Possible side effects of 10%Phenylephrine eye drops are tachycardia, high blood pressure, headache and dizziness.^{3,4} Nevertheless, the conventional technique for pupil dilation requires multiple alternating eye drops of 1%Tropicamide and 10%

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Phenylephrine, applied every 5 minutes; so the patients may frequently feel irritation in their eyes. Moreover, numerous staff or nurses involved in several steps of applying eye drops may be a cumbersome process with potential unexpected human errors. Thus the purpose of this study was to evaluate the pupil diameter and irritative symptoms of mydriatic drug-soaked sponge packing versus conventional instillation technique in the patients who need fundus examination.

Methods

This study was reviewed and approved by Thammasat University Ethics Committee for human research. The sample size was calculated from formula which estimated the number of patients per treatment group to be 40.5. The patients were recruited from the outpatient department of Thammasat University Hospital from October 2017 to January 2018. Written informed consent was obtained from all patients. Inclusion Criteria: Patients aged 18 to 80 years old who require pupil dilation for fundus examination. Exclusion Criteria: Patients allergic to mydriatic drugs, previous intraocular surgery, ocular trauma, abnormal iris, previous uveitis, history of closed angle glaucoma, intraocular pressure more than 21 mmHg, abnormal size of pupil diameter, pupil irregularity, blindness, unconsciousness and uncooperative patients. The patients were randomized to either conventional instillation or mydriatic soaked sponge at the lower conjunctival fornix in one eye and the other technique in the other eye. Measure the size of pupils' diameter in horizontal line with slit lamp. Soaked-sponge (polyvinylalcohol) technique:

- Cut sponge size to 2 mm x 10 mm x 3 mm
- One drop of 1% Tropicamide, followed by 1 drop of 10% Phenylephrine, 3 times on the sponge
- One drop of 0.5% Tetracaine at the lower conjunctival fornix
- Place the mydriatic drug-soaked sponge

on the lower conjunctival fornix, then remove it after 20 minutes.

e. Measure pupil diameter at 10, 20 and 30 minutes

Conventional technique:

- One drop of 0.5% Tetracaine at the lower conjunctival fornix
- One drop of 1% Tropicamide at the lower conjunctiva then after 5 minutes, one drop of 10% Phenylephrine at the lower conjunctiva. Alternating between these two drugs every 5 minutes for 20 minutes.

The irritative symptoms score were monitored after completing both techniques which scale from 1 to 10 (10 being the worst). In the evaluation of this study; a comparison of the mydriatic effect and irritative symptoms of lower conjunctival fornix between using mydriatic drug soaked sponge versus conventional technique. The data were analysed using a t-test to compare the irritative symptom of both groups statistical significant was taken as $p < 0.05$.

Results

Forty patients were recruited in this study. The proportion of gender and mean age were similar in both groups (table 1).

The mean pupil diameter at baseline was 2.0 ± 0.3 in both groups and after mydriatic drugs application at 10, 20 and 30 minutes were 3.2 ± 1.0 , 5.5 ± 1.3 and 7.0 ± 1.1 mm respectively. Mean pupil diameter for soaked sponge technique was 3.2 ± 0.8 , 5.4 ± 1.1 and 6.5 ± 1.0 mm respectively ($p = 0.661$, 0.682 , 0.974) (table 2) (figure 1).

The proportion of pupils dilated greater than 7mm at 20 and 30 minutes were 5.13% and 51.35% in the drug soaked sponge technique group and 2.63% and 41.03% in the conventional technique group ($p = 0.718$ and 0.822) respectively (table 3). The irritative symptom scores were 4.9 ± 2.6 and 3.0 ± 2.4 in mydriatic drug soaked sponge group and conventional group respectively ($p = 0.0006$). (table 4)

Table 1: Demographics comparison mydriatic drug soaked sponge technique versus conventional technique.

Variables	Drug soaked sponge technique(N=40)	Conventional technique (N=40)
Gender	Male : 35.0% Female : 65.0 %	Male : 35.0% Female : 65.0 %
Age (Mean \pm SD)	58.8 \pm 10.5	58.8 \pm 10.5

Table 2: Diameter pupil diameter average by technique and time

Time (minute)	Mean pupil diameter (mm) \pm SD		P-value
	Mydriaticdrugsoaked sponge technique	Conventional technique	
0	2.0 \pm 0.3	2.0 \pm 0.3	0.446
10	3.2 \pm 1.0	3.2 \pm 0.8	0.661
20	5.5 \pm 1.3	5.4 \pm 1.1	0.682
30	7.0 \pm 1.1	6.5 \pm 1.0	0.974

Table 3: Comparison mydriatic drug soaked sponge technique versus conventional technique in terms of percentage dilated pupil (≥ 7 mm)

Pupil dilation time (minutes)	Proportion of pupils dilated (≥ 7 mm)		P-value
	Mydriaticdrugsoaked sponge technique	Conventional technique	
0	0.00%	0.00%	-
10	0.00%	0.00%	-
20	5.13%	2.63%	0.718
30	51.35%	41.07%	0.822

Table 4: Irritative symptom (score)

Variables	Mydriatic drug soaked sponge technique (Mean \pm SD) (N=40)	Conventional technique (Mean \pm SD) (N=40)	P-value
Irritative symptom (score 1-10)	4.9 \pm 2.6	3.0 \pm 2.4	0.0006

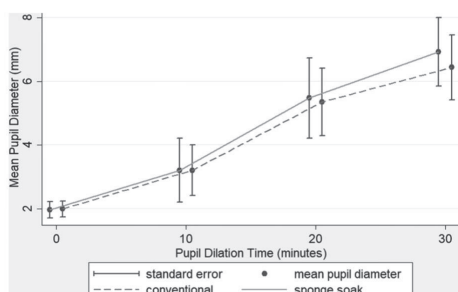


Figure 1: Comparison of mydriatic drug soaked sponge versus conventional technique of pupil dilation.

Discussion

In most cases, patients requiring posterior segment evaluation by fundus exam should have pupil diameters of approximately 7 mm or greater. Typically, the regular dilatation method is the conventional technique of repeating instillations of two mydriatic drugs, however this technique has a high turnover of fluid at cul-de-sac about 16% per minute and then 50% at 4 minutes; thus, the alternating eye drops are essential every 5 minutes. Therefore in this study we used the mydriatic drug soaked sponge placing at the inferior fornix instead of repeating instillation. The type of sponge was polyvinylalcohol (PVA) which constructed from ultra-smooth micro-pore PVA sponge, have ultra-fast wicking action and is suitable for tissue manipulation. In this study, the mean pupil diameter from mydriatic drug soaked sponge technique and conventional technique were not significantly different at 20 and 30 minutes. While the proportion of acceptable pupil diameter ($\geq 7\text{mm}$)⁶⁻⁸ at 20 and 30 minutes were also not significantly different. These findings were similar to Dubois et al⁶ and McCormick et al⁷ that showed no significant difference in providing mydriasis between mydriatic drug soaked depot delivery or pledget soaked placed in the lower fornix and conventional repeated drop administration in patients for cataract surgery. However in our study, the mean

pupil diameter and the proportion of acceptable pupil diameter at 30 minutes were slightly higher in mydriatic drug soaked sponge group than the conventional group. This higher effect may be from the increasing contact time of mydriatic drug which soaked by sponge at lower fornix. Nonetheless, these differences were not statistically significant.

The irritative symptom score of mydriatic drug soaked sponge was significantly higher than the conventional technique. Based on patient feedback, they felt that the soaked sponge similar to foreign body in their eyes, however there was no such cases requested for sponge removal before 20 minutes.

The limitation in this study was at 30 minutes the proportion of acceptable pupil diameter (more than 7 mm) was 51.35% by drug soaked sponge technique and 41.07% by conventional technique. Our data has shown that almost half of all eyes could not achieve the acceptable pupil diameter in both techniques. Possibly, the drug may not take full advantage of its maximum effect which may take longer time or additional drug for those patients to have wider pupil diameter.

In conclusion, the mydriatic drug soaked sponge technique can provide mydriatic effects similar to the conventional instillation technique. The sponge technique uses less staff and can improve the efficiency of any clinical setting. Nevertheless, this technique can cause significant irritation or foreign body sensation in some patients.

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The relationship of age at surgical alignment and the development of stereopsis in infantile esotropia

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Objective: To determine the power of the stereopsis and the relationship between the development of stereopsis and age at surgical alignment in patients with infantile esotropia. **Methods:** A cross sectional study on 110 children with infantile esotropia who underwent a single operation from 1/1/2011 to 1/1/2014 and had alignment within 10 PD of orthotropia at all follow-up examinations. Stereopsis was assessed by the Original Randot Stereotest.

Results: The mean age at surgery was 36.79 ± 16.05 months (range, 16–72 months). The percentage of patients having stereopsis was 30.9% (34 patients). 26 patients operated at 16–24 months (68.42%) and 8 patients operated at 24–48 months (20.51%) had stereopsis. No patient operated after 39 months had stereopsis. There was a statistically significant correlation between age at surgery and final stereopsis ($r_s = 0.649$; $p < 0.001$). Receiver operating characteristic curve analysis revealed that the optimum cut-off value of the age at surgery for predicting stereopsis was 21.5 months (Youden index = 0.378; area under ROC curve = 0.827; 95% CI: 0.74–0.92; $p < 0.001$).

Conclusion: Age at surgery plays an important role in the development of stereopsis. Surgery for infantile esotropia is most likely to result in measureable stereopsis if patient age at alignment is not more than 21.5 months.

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

Keywords: infantile esotropia, stereopsis.

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Introduction

Strabismus is a syndrome defined by the difference between the visual axis of one eye to another, which affects the movements and functions of the eyes. One form of strabismus that can directly and seriously affect the visual function of children if not treated soon is infantile esotropia. This form of strabismus makes up 0.25% of infants and usually accompanies with abnormal binocular visual function of their

eyes.⁵ In 1939, Chavasse brought up a theory that the cause of unusual binocular vision of children with esotropia an onset of esotropia before the age of 6 months, known as infantile esotropia, was due to the presence of esotropia during the children's binocular vision developing period. This theory guided the clinicals to the decision to perform the alignment surgery early, hoping to recover the binocular vision of patients. However, the optimum age for corrective surgery in children with infantile esotropia remains controversial. The purpose of this study is to determine the correlation between the development of binocular vision and the age of align-

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ment surgery to determine the optimal age of surgical intervention in children with infantile esotropia.

Methods

Subjects : The patients undergoing a single surgery for infantile esotropia were followed up at Ho Chi Minh Eye Hospital from 1/1/2011 to 1/1/2014.

Methods : Inclusion criteria for this study were as follows: (1) Infantile esotropia patients who had surgery from 1/1/2011 to 1/1/2014, (2) Final alignment within 10 PD of orthotropia, (3) Visual acuity between two eyes differ ≤ 2 lines, (4) Best corrected visual acuity $\geq 3/10$.

Children with conditions such as preoperative amblyopia, manifest or latent nystagmus, anisometropia >1.5 D, limitations in abduction consistent with Duane syndrome or abducens nerve palsy, and patients with neurologic defects, meningitis, or other major medical conditions were excluded.

Initial measurements were performed with a prism-and-cover test if possible or by means of the Krimsky method. All patients with histories of constant-angle esotropia before 6 months or a diagnosis of infantile esotropia by an ophthalmologist before 8 months of age were accepted as having infantile esotropia, following the inclusion criteria described in a study by Birch and colleagues. All patients had

only one bilateral medial rectus recession procedure; inferior oblique tenotomy performed during the same operation for inferior oblique overaction was recorded and investigated for the association with the later stereopsis. Patients identified by record review were recalled and examined for stereopsis which was assessed using the Randot test.

Results were analyzed using SPSS version 20 (SPSS Inc, Chicago, IL). All statistical tests were 2-sided; the threshold of significance was $p \leq 0.05$. The Mann-Whitney test was used to compare between two groups, and a statistical evaluation of the correlation was performed using the Spearman test because of the ordinal scale of the stereopsis power in the Randot test. The ROC curve analysis was performed to determine whether results would have changed had success been defined as alignment to within 10 PD of orthotropia.

Results

1. The particular traits of the samples
Within the duration of this study from December 2016 to June 2017 at our Strabismus Clinic in Ho Chi Minh City Eye Hospital, we have chosen 110 children within the inclusion criteria, all of which have consent from their parents to participate in the study.

Ages at surgery

Table 1: Age of the patients in this study

Characteristic (months of age)	N	Percentage (%)
Age at surgery		
16 – 24 months	38	34.55
24 – 48 months	39	35.45
48 – 72 months	33	30
Average \pm standard deviation	36.79 \pm 16.05	
Youngest – eldest	16-72	

The children's ages at surgery in this study were categorized into 3 groups (table 1). The numbers of the children in each group were similar across all groups.

Characteristics of participants

Table 2: Characteristics of participants

Post operative characteristics Angle of esotropia (PD)	N	Percentage (%)
0 PD	67	60.9
8 PD	31	28.2
10 PD	12	10.9
Spherical equivalent (D)	1.58 ± 0.91 (0 ± 5.75)	

Binocular vision

Children who developed stereopsis consisted of only 1/3 of the study sample (34 children, equivalent to 30.9%).

Figure 1: Describes stereopsis rate in groups of children experiencing esotropia with different surgical ages.

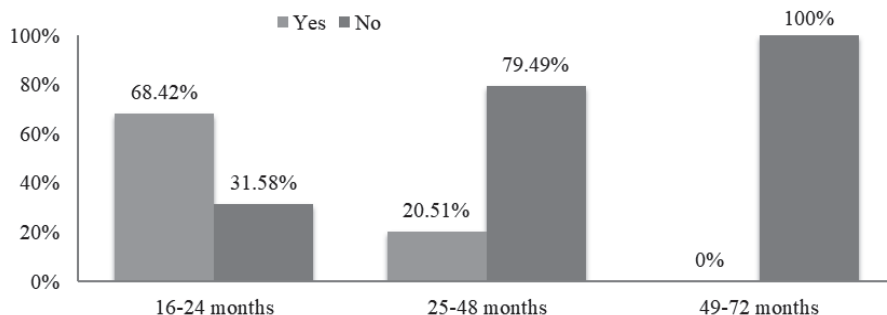


Figure 1: Stereopsis rate in different surgical age groups

In the group with age at surgery between 16 and 24 months, 26 children (68.42%) developed visual stereopsis. Meanwhile, only 8 children (20.51%) between 24-48 months old had stereopsis. All the children who had alignment surgery after 39 months did not demonstrate stereopsis. The average stereopsis of the research

group was 841.82 ± 249.91 arcsec (200-1000 arcsec). Most patients demonstrated stereopsis of 600 arcsec (19 children with the ratio of 55.88%).

2. The correlation between binocular vision and age at surgery

In the group with age at surgery between 48-75 months (n=33), all patients did not have stereopsis, so we only chose children with the age at surgery less than 48 months (n=77) to investigate the correlation between binocular vision and the surgery age.

Figure 3 demonstrated the correlation between the stereopsis rate and the age at surgery of the children with onset of esotropia

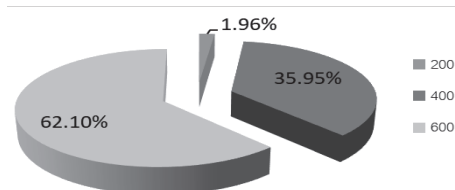


Figure 2. Stereopsis rate of the sample

before age 6 months. Patients that do not develop the defined visual stereopsis with stereoacuity of 1000 arcsec. Stereoacuity of the patients in the study group had a statistically significant correlation with the age at surgery (Spearman correlative index $r_s = 0.649$; $p < 0.001$).

In order to find the age at surgery to help anticipate the development of stereopsis, we analyzed the ROC receiver operating curve.

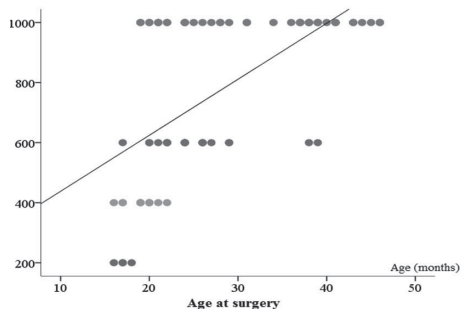


Figure 3: Scatter diagram of the stereopsis by the age at surgery

The analysis result of the ROC (receiver operating curve) showed that the age at surgery can predict the existence of the stereopsis (area under ROC was 0.827; 95% CI: 0.74-0.92; $p < 0.001$). The cut-off value for predicting stereopsis was 21.5 months old (Youden index = 0.378; sensitivity = 83.7%; specificity = 52.9%).

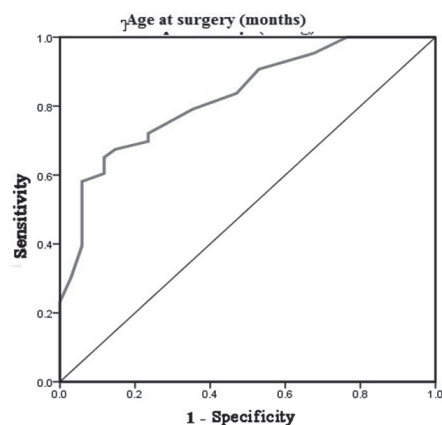


Figure 4: ROC curve between age at surgery and stereopsis

Discussions

1. Particular characteristics of the sample : age at surgery

The average age at surgery as well as the proportion of children with infantile esotropia having alignment surgery after the age of 24 months in our research was higher than those of Simonsz (2005) and Cerman (2014).^{3,6} This difference suggests that with time, the progress of surgical techniques and anesthesia, the children's age of alignment surgery has gradually reduced to improve the rate of binocular vision development.

However, because the children with infantile esotropia came to the clinic with an underweight condition, and due to their parents' lack of ability to take care of the children after the anesthesia surgery, the smallest age at surgery at our Strabismus Clinic was 20 months old.

Binocular Vision

Of the 110 children enrolled in this study, 34 developed stereopsis, equivalent to 30.9%. Compared to the research of Birch (2000), Ing (2002) and Cerman (2014), the proportion of stereopsis in our research is lower than that of other authors' research.^{1,3,4} In particular, Birch also investigated the development of stereopsis using the Randot test, however, the author only studied children with surgery ages of ≤ 24 months. The rather high proportions of stereopsis in Ing's and Cerman's research might be due to the presence of partial stereopsis when assessing stereopsis with Titmus test and TNO test.

The proportion of < 200 arcsec stereopsis in the research was 6.9%. This number is relatively low, comparing to the result of Birch's research (2006, 20%).² This difference was perhaps because Birch did research on children aligned before 6 months old.

2. The correlation between binocular vision and the age at surgery

There was a statistically significant corre-

lation between the quality of stereo acuity and the age at surgery (Spearman correlative index $r_s = 0,649$; $p < 0.001$). Birch's research in 2000 also concluded that the patients' age at the time of alignment was statistically correlative with the stereo acuity (Spearman correlative index $r_s = 0,41$; $p < 0.001$).¹ Hence, children with infant esotropia need aligning earlier in order to gain highest quality of stereopsis. Achieving this goal requires cooperation between ophthalmologists and the centers of health communication and education in propagating and advising parents about the children having infantile esotropia, the harms brought by the strabismus condition and the benefits of early surgery to the development of visual function of the children. The result of ROC curve analysis showed that the age at surgery could predict the development of binocular vision (area under the ROC curve is 0.827; 95% CI: 0.74-0.92; $p < 0.001$) The cut-off value of the age at surgery to predict the presence of stereopsis is 21.5 months old (Youden index = 0.378; sensitivity = 83.7%; specificity = 52.9%). Hence, surgery at the age before 21.5 months may help children with infantile esotropia achieve the best stereopsis. Cerman and partners (2014) also concluded that ROC curve is valuable in predicting the age at surgery that can increase the proportion of children with infantile esotropia achieving stereopsis (area below the curve was 0.784; 95% CI: 0.62 – 0.90; $p < 0.001$). The cut-off value of the age at surgery in Cerman's research was 16 months old (Youden index = 0.474; sensitivity = 63.2%; specificity = 84.2%). The difference between this two research was due to the fact that the children in Cerman's research had smaller age at surgery comparing to those in ours; while the former study's youngest age at surgery was 7 months, the latter was 16 months.

Conclusion

Age at surgery plays an important role

in the development of binocular vision of children with infantile esotropia. The proportion of stereopsis highly increases when the children have undergone surgical correction before the age of 21.5 months.

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