EVALUATION OF THE CHANGES OF ANTERIOR SEGMENT BIOMETRY AND INTRAOCULAR PRESSURE IN PATIENTS TREATED WITH INTRAVITREAL INJECTION OF ANTIVASCULAR ENDOTHELIAL GROWTH FACTORS

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DISCLAIMER

I hereby certify that the work in this dissertation is my own except for the quotations and summaries which have been duly acknowledged. I declare that I have no financial interest in the instruments in this study.

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Abstract

Introduction: Anti-vascular endothelial growth factors (anti-VEGF) intravitreal injection is one of the popular procedures for medical retina diseases. However, this common procedure does associate with ocular side effects of which raised intraocular pressure (IOP) is the commonest. This study aimed to evaluate the changes of anterior segment biometry with IOP post intravitreal injection. **Materials and Methods:** From May 2020 till May 2021, this prospective cohort study recruited 72 eyes of 66 patients who received intravitreal injection of either Aflibercept or Ranibizumab. Recruited candidates were examined for IOP and anterior segment biometry using Visante "anterior segment-optical coherence tomography" (AS-OCT) before and after injection. The anterior segment biometry measured in this study includes central anterior chamber depth, angle opening distance at nasal and temporal (AOD500 nasal, AOD500 temporal), and trabeculo-iris angle at nasal and temporal (TIA500 nasal and TIA500 temporal). **Results:** Mean (SD) increment of IOP following injection within 30 minutes and 1 hour were 6.16 (0.68) mmHg ($p<0.001$) and 1.26 (0.35) mmHg ($p=0.002$) respectively. Mean (SD) differences of TIA500 temporal between pre with within 30 minutes and 1-hour post-injection were 1.66 (0.66) degrees ($p=0.04$) and 1.45 (0.57) degrees ($p=0.04$) respectively. The changes of other anterior segment biometry parameters were not significant. Also, no significant relationship between IOP changes and anterior segment biometry was found. **Conclusions:** A single dose of intravitreal anti-VEGF injection is associated with short-term raised in IOP. There are no significant changes in anterior segment biometry parameter except for TIA500 temporal and it has no statistically significant relationship with IOP changes post intravitreal anti-VEGF.

Abstrak

Pendahuluan: Suntikan intravitreal “anti-vascular endothelial growth factor” (anti-VEGF) adalah rawatan popular untuk penyakit perubatan retina. Walau bagaimanapun, prosedur ini mempunyai beberapa kesan sampingan okular dimana peningkatan tekan intraokular (IOP) adalah yang paling biasa. Kajian ini bertujuan untuk menilai perubahan biometri okular dengan IOP. **Bahan dan Kaedah:** Dari Mei 202 hingga Mei 2021, 72 mata daripada 66 pesakit yang menerima suntukan intravitreal 0.05 ml sama ada aflibercept atau ranibizumab telah dipilih ke dalam kajian kohort prospektif ini. Pesakit telah diperiksa untuk IOP dan anterior segmen biometri menggunakan Visante “anterior segment-optical coherence tomography” (AS-OCT) sebelum dan selepas suntikan. Anteior segmen biometri yang diukur termasuk jarak ruang hadapan mata, jarak bukaan sudut “nasal” dan “temporal” (AOD500 nasal, AOD500 temporal), dan sudut trabeculo-iris “nasal” dan “temporal” (TIA500 nasal, TIA500 temporal). **Keputusan:** Purata kenaikan IOP selepas suntikan dalam masa 30 minit dan 1 jam adalah 6.16 (0.68) mmHg ($p<0.001$) dan 1.26 (0.35) mmHg ($p=0.002$). Perbezaan min (SD) TIA500 antara pra-suntikan dengan tempoh 30 minit serta 1 jam selepas suntikan ialah 1.66 (0.66) darjah ($p=0.04$) dan 1.45 (0.57) darjah ($p=0.04$). Tiada hubungan antara perubahan IOP dan biometri okular dikesan. Perubahan parameter anterior segmen biometri lain adalah tidak ketara. **Kesimpulan:** Satu dos suntikan anti-VEGF boleh menyebabkan peningkatan IOP dalam jangka pendek. Tiada perubahan ketara dalam anterior segmen biomteri kecuali “TIA500 temporal” dan ia tidak mempunyai hubungan dengan perubahan IOP selepas suntikan anti-VEGF. Kajian lanjut melibatkan populasi yang berpenyakit dan suntikan berulang adalah bermanfaat.

Chapter 1
Introduction

1.1 Intravitreal antivascular endothelial growth factors (anti-VEGFs)

Intravitreal antivascular endothelial growth factors is getting more and more popular nowadays (1). In United States, several million anti-VEGF injections are administered every year and this number is increasing (2). The VEGF family of proteins includes VEGF-A, VEGF-B, VEGF-C, VEGF-D and VEGF-E, and placental growth factor (3). Vascular endothelial growth factor (VEGF) is playing a role in the pathogenesis of age-related macular degeneration (AMD) and other etiology of choroidal neovascularisation (CNV) such as retinal vein occlusion, pathological myopia and uveitis (4, 5). AMD and this vascular condition can be treated with anti-VEGF. The available anti-VEGF are Pegaptanib, Ranibizumab, Bevacizumab and Aflibercept (4). AMD has a global prevalence of 170 million. Thereby it is the third leading cause of visual disability globally (6).

Ranibizumab (Lucentis, Genentech, Inc., South San Francisco, CA) is a 48-kilodalton (kDa) recombinant humanized immunoglobulin G1 kappa isotype antibody fragment. It binds to all isoforms of VEGF-A and thus suppresses neovascularization (7).

Aflibercept (EYLEA, Regeneron Pharmaceuticals, Inc., Tarrytown, NY), previously known as VEGF Trap-Eye, is a 115-kDa recombinant fusion protein consisting of VEGF extracellular binding domains of the human VEGF receptors 1 and 2 fused to the Fc domain of human immunoglobulin G1. It is a competitive inhibitor of VEGF and also binds placental growth factors 1 and 2 (7). Aflibercept binds multiple isoforms of human VEGF-A, VEGF-B, and placental growth factor (8).

Anti-VEGF therapy has been administered at regularly spaced fixed intervals in ‘continuous’ regimens or at varying intervals in ‘discontinuous’ regimens to reduce the burden, risks and costs of repeated intravitreal injections. These discontinuous regimens include a ‘pro re nata’ (PRN) approach based on findings of exudation, or a ‘treat and extend’ (T&E) approach that gradually increases assessment and treatment intervals after exudation is controlled (3).

1.2 Intraocular pressure (IOP)

The fluid pressure of the eye is known as intraocular pressure (IOP). The Goldmann equation, which is IOP = (F/C) + P, where F is aqueous flow rate, C is aqueous outflow, and P is the episcleral venous pressure is used to determine the IOP theoretically. The IOP is measure by the force exerted by the aqueous humor on the internal surface area of the anterior eye. Changes and alterations of these variables will affects the IOP (9).

Aqueous humor play an important role in intraocular pressure. Aqueous humor is produced in ciliary body within the posterior chamber of the anterior eye. It accumulates in posterior chambers and flows to anterior chamber through the pupil. Aqueous humor exits the anterior chamber via three routes. Most of the it drains out from anterior chamber through the angle at trabecular meshwork and into Schlemm canal which then enters episcleral veins. On the other hand, small amount of aqueous humor drains into suprachoroidal space and enters venous circulation in the ciliary body, choroid and sclera. Lastly, very small amount of aqueous humor drains through iris and into posterior chamber (9).

The variation of intraocular pressure can be extreme with nocturnal or diurnal IOP peals. In normal individuals, the mean IOP is 14.7 ± 2.8 mmHg. (10) Normally, IOP fluctuation typically lies within a 5 mmHg range in healthy normotensive eyes. IOP oscillation exhibits peaks in the morning and troughs in the evening (11).

In a Singapore epidemiology of eye diseases study, they evaluated on ethnic differences of intraocular pressure. The mean IOP readings in the Chinese, Malay, and Indian participants were 14.3±3.1, 15.3±3.7, and 15.8±2.9 mmHg, respectively ($P < 0.001$) (12).

Sudden increases in IOP can cause and ischemic effects and mechanical stress on the retinal nerve fiber layer (9). The major risk factor of onset and progression of glaucoma is elevated intraocular pressure (IOP). Moreover, elevated IOP causes oxidative stress, inflammation, and consequently tissue damage in the retina and optic nerve (13).

1.2.1 IOP post intravitreal injection anti-VEGFs

Gul Arikan et al. studied on immediate intraocular pressure rise after intravitreal injection of ranibizumab and two doses of triamcinolone acetonide. They divided patient into three groups. Patient who underwent intravitreal injection of 0.1mL (4mg) triamcinolone acetonide (TA, Group T4), 0.05mL (2mg) (TA, Group T2) and 0.05mL (0.5mg) ranibizumab (Group R). In this study they found that, there is immediate rise of IOP over 25mmHg, where 51.9% in group T4, 31% in group T2 and 48.1% in group R respectively. At 30 minutes, IOP of 1.9% in group T4, 2.9% in group T2 and 1.9% in Group R were over 25mmHg (14).

Although it was acute IOP spike, but it may lead to negative effect on ocular circulation as high IOP may compromise central retinal artery blood flow and/or the optic nerve head and hinder axonal transport. Nevertheless, patient with glaucomatous optic nerve will even more susceptible to the damage (14).

The transient elevation of intraocular pressure after intravitreal anti-VEGF injection is because of temporary increase in intraocular volume, and this acute spike generally does not affect a healthy eye. Persistent elevation of intraocular pressure is more common than previously thought. This persistent rise may be correlated to several factors including increased number of intravitreal injections (15). There is significant increase in IOP after injections of bevacizumab and ranibizumab. However, the increase was limited and did not exceed 30mmHg (16).

Hoquet A. et al did a summary report of various study on the effect of anti- VEGF on IOP and glaucoma. Fourteen studies reported on short-term pressure effects of anti-VEGF injections. Among the studies, 100% of patients had an increase in IOP. Studies found that the IOP decreased over time, where at 30 minutes mean IOP range from 17.6 to 24.5mmHg. In majority of patients, IOP returned to normal within a short period of time, typically within 1 hour (17).

Sudden rise in IOP post intravitreal injection of anti-VEGF could be due to sudden increase volume of the orbit and the rigidity of the scleral (18). On the other hand, Aaron Ricca suggested that the raised IOP post intravitreal anti-VEGF is related to the alteration of nitric oxide synthase. Nitric oxide in anterior chamber helps in increase aqueous outflow by reducing trabeculocyte size, dilating Schlemm's canal and relaxation of smooth muscle. VEGF reduces nitric oxide resulting in decreased aqueous outflow (19).

The incident of high IOP is also related to the number of injections. The higher the number of injections the higher the risk of sustained IOP post anti-VEGF injections (20). Sustained high IOP also found in patient treated with multiple intravitreal bevacizumab injections (21).

1.3 Anterior segment biometry

Several anatomic parameters that can be measured by OCT, including trabecular-iris angle (TIA), angle opening distance (AOD) and trabecular-iris space area (TISA). These have been identified as a more accurate and objective method of assessing the iridocorneal angle (22). In this study we are going to measure 3 anterior segment biometry which are anterior chamber depth, trabecular iris angle and angle opening distance. (Figure 1)

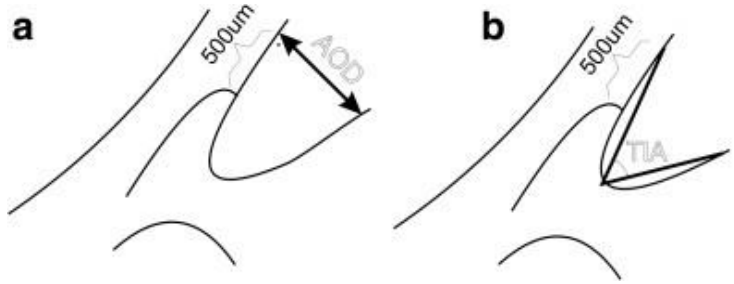

Figure 1. a) AOD 500 (Angel Opening Distance) involves measuring a distance between a point of the cornea which is 500 μm away from the scleral spur and the opposite point of the iris. b) TIA (Trabecular-Iris Angle) involves a direct measurement of the angle.

1.3.1 Anterior chamber depth (ACD)

The anterior chamber depth (ACD) is the distance between the anterior surface of the cornea and the anterior surface of the lens (23). Normal population has ACD of 2.84mm ± 0.46 measure by IOLMaster and 3.02mm ± 0.46 measure by ultrasound. (24) There are study showed that shallower ACD measurements in females compared to males, independent of instrument or technique. They hypothesized it is because of smaller anthropomorphic measurements. Asian eyes has a tendency to have shallower ACD (25).

1.3.1.1 ACD post intravitreal injection anti-VEGFs

Gurcan Dogukan Arslan et al. evaluate the short-term changes in ACD, central cornea thickness, IOP, and corneal endothelial cell density after intravitreal anti-VEGF injection. They found that mean ACD of all eyes and phakic eyes was significantly lower one month after the first ($p < 0.001$ and $p < 0.001$, respectively) and second injections ($p < 0.001$ and $p < 0.001$, respectively) compared to the values at pre-injection levels. However, there was no significant difference of the mean ACD in pseudophakic eyes one month after the first and second injections (26).

There is a study conducted in Turkey by Alkin A et. al., they evaluated the effects of 2 different amounts of commonly used intravitreal agents on anterior segment morphology in conjunction with intraocular pressure. They divided the population into two groups which are bevacizumab (group 1, 0.05mL) and bevacizumab-triamcinolone acetate (TA) combination (group 2, 0.1mL). There was a statistically significant difference from baseline in ACD at the first and second measurements in group 2 ($p = 0.005$, $p = 0.018$, respectively) (27).

1.3.2 Trabecular Iris Angle (TIA)

The trabecular-iris angle (TIA) was defined as an angle measured with the arms of the angle passing through a point on the trabecular meshwork 500 μm from the scleral spur and the point on the iris perpendicularly (28). TIA of temporal quadrant was averaged at 35.8 ± 12.2 degrees (range 1.5 to 76.1) while the nasal quadrant was averaged 35.7 ± 12.3 degrees

(range 2.2 to 74.8) using Fourier Domain optical coherence tomography (OCT). Men's TIA found to have 4.49 degrees greater than in women.(22) The mean TIA was found to be 35.5 ± 9 degrees with the OCT Visante (time domain OCT) by Wylegala et al (29).

1.3.2.1 TIA post intravitreal injection anti-VEGFs

El Chehab H et al. conducted a study on intraocular pressure (IOP) as well as the anatomical modifications of anterior segment following an aflibercept injection. All patients underwent an aflibercept intravitreal injection of 0.05ml. Anterior chamber parameters (anterior chamber volume, depth and measure of iridocorneal angle) was evaluated by pentacam before injection and immediate after injection. There were no significant changes were found for iridocorneal angle (30). Pentacam has promising technology providing rapid and reproducible measurements of anterior chamber. It has rotating camera which takes images from numerous data points in 2 seconds after 180-degree rotation. It gives three dimensional reconstruction of the anterior segment, information, and quantify anterior chamber depth and anterior chamber volume using colored map (31).

1.3.3 Angle opening distance (AOD)

The AOD 500 was defined as the distance from the corneal endothelium to the anterior iris surface perpendicular to a line drawn at 500 μm from the scleral spur. (28) Normal nasal AOD was found to be 435μm ± 95 while temporal AOD was 443μm ± 103 measured using time-Domain OCT (29).

1.3.3.1 Angle opening distance post injection anti-VEGFs (AOD)

Joanne C Wen et al. studied on pre and immediate post injection IOP and AS-OCT. The results showed that the mean (±SD) differences between pre- and post-injection images of the temporal angle were: 0.05±0.11 mm (AOD500) (p=0.03), 0.07±0.13 mm (AOD750) (p=0.01) However there was no significant difference between pre- and post-injection image

measurements of the nasal angle. A higher post injection IOP was correlated with increased narrowing of the nasal AOD500 (R = 0.02 and P = 0.03)(32).

Alkin Z et. al. study found that there was insignificant decrease of AOD 500-750 from baseline at measurement of 5 minutes, 1 hour and 3 hour after injection of bevacizumab (0.05mL) and bevacizumab-triamcinolone acetate combination (0.1 mL) (27).

1.4 Anterior segment optical coherence tomography (AS-OCT).

Optical coherence tomography (OCT) is a modality that uses low-coherence interferometry to enable non-contact, *in vivo* imaging of ocular structures (33). Anterior segment OCT (ASOCT) imaging was first described in 1994 by Izatt et al using the same wavelength of light as retinal OCT, namely 830nm (34). However it is suboptimal to visualize anterior segment structure such as the angle due to limited penetration through sclera. Later, OCT with longer wavelength of 1340nm has a better penetration through sclera (34). Currently, there are two AS-OCT models commercially available which are the ZEISS Visante™ OCT Model 1000 (Visante OCT) (Carl Zeiss Meditec, Dublin CA, USA) and the Slit-Lamp OCT (SLOCT) (Heidelberg Engineering, GmbH, Dossenheim, Germany) (35).

The Visante OCT has several scanning protocols of which are the High Resolution Raw scan and the Enhanced Anterior Segment Single Scan are most useful for anterior segment assessment (34). Its axial and transverse image resolutions are up to 18 and 60 μm and has scan rate reaches up to 2000 A-scans per second (33).

Qualitative and quantitative assessment of anterior chamber angle (ACA), anterior chamber, iris and lens can be identify with AS OCT. Angle closure with AS OCT is determined by any contact between the iris and the angle wall anterior to the scleral spur. The common parameters used to describe features of the ACA include the angle recess area (ARA), the angle opening distance (AOD), and the trabecular-iris space area (TISA) (33).

1.5 Rationale of study

Intravitreal anti-VEGF agents have been revolutionized and widely used in vitreoretinal and medical retinal practice all around the world in recent years. Although only small volume of 0.05ml of anti-VEGF agent was given, the increased of orbital fluid volume post intravitreal injection causes significant changes in IOP. The acute rise in volume causes changes in intraocular fluid dynamics and anterior chamber morphology especially in the absence of reflux (27).

Acute rise in IOP can gives ischemic effects and mechanical stress on the retinal nerve fiber layer leading to glaucoma and blindness (9). Hoquet A. et al did a summary report of various study on the effect of anti- VEGF on IOP and glaucoma. Fourteen studies reported on short-term pressure effects of anti-VEGF injections. Among the studies, 100% of patients had an increase in IOP. Studies found that the IOP decreased over time, where at 30 minutes mean IOP range from 17.6 to 24.5mmHg. In majority of patients, IOP returned to normal within a short period of time, typically within 1 hour (17).

Exact pathophysiology of raise IOP post intravitreal injection of anti-VEGF is still unknown. Due to rigidity of the scleral, when the volume enters the vitreous cavity, it probably pushing forward to the anterior chamber and causes change in anterior segment morphology. It may then cause sudden obstruction in aqueous outflow.

Unfortunately, previous studies done on anterior segment biometry post intravitreal injection of anti-VEGF were inconclusive and none of them explore the relationship of IOP and anterior segment biometry changes. Nevertheless, variable ocular biometric parameters were reported between Asians and Caucasians where angle recess area, anterior chamber width, iris curvature and thickness were found among Caucasians as compared to Chinese population (36). No similar study was conducted on the perspective of biometry changes in Malaysia and limited study in Asian countries. Furthermore, variable baseline IOP was identified among

different ethnicity as well, of which Chua J et al from Singapore reported of mean IOP of 14.3±3.1 mmHg, 15.3±3.7 mmHg, and 15.8±2.9 mmHg among the Chinese, Malay, and Indian participants respectively (12).

This urge for local studies for better understanding regarding the anterior segment biometry changes and risk of developing high IOP following intravitreal injection of anti-VEGF among our local multiracial population. We used the common anti-VEGF used recently which is ranibizumab and aflibercept. ASOCT which the best tool to measure anterior segment morphology is used in this study.

By conducting this study, it aids us in understand more on the anterior segment biometry changes after intravitreal injection of anti-VEGF and help in preventing acute angle closure attack by giving pre-medication or medication after intravitreal injection of anti-VEGF.

This study also can be used as a reference in future for other study regarding intravitreal injection of anti-VEGF especially on the anterior segment biometry.

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Chapter 2
Objective of the study

2.1 General Objective

To evaluate the changes of anterior segment biometry and intraocular pressure (IOP) in patient treated with intravitreal injection of anti-vascular endothelial growth factors (anti-VEGF).

2.2 Specific Objectives

1. To determine the IOP changes within 30 minutes and at 1 hour post intravitreal injection of anti-VEGF.

2. To determine the anterior segment biometry (anterior chamber depth, nasal and temporal trabeculo-iris angle at 500 µm, nasal and temporal angle opening distance at 500 µm) changes within 30 minutes and at 1 hour post intravitreal injection of anti-VEGF.

3. To determine the relationship of the anterior segment biometry (anterior chamber depth, nasal and temporal trabecular iris angle at 500 µm, nasal and temporal angle opening distance at 500 µm) with the IOP difference within 30 minutes and at 1 hour post intravitreal injection of anti-VEGF.

Chapter 3
Manuscript

3.1 Title Page

TYPE OF MANUSCRIPT: Original article

Changes of anterior segment biometry and intraocular pressure in patients treated with intravitreal injection of antivascular endothelial growth factors

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3.2 Abstract

Introduction: Anti-vascular endothelial growth factors (anti-VEGF) intravitreal injection is one of the popular procedures for medical retina diseases. However, this common procedure does associate with ocular side effects of which raised intraocular pressure (IOP) is the commonest. This study aimed to evaluate the changes of anterior segment biometry with IOP post intravitreal injection. **Materials and Methods:** From May 2020 till May 2021, this prospective cohort study recruited 72 eyes of 66 patients who received intravitreal injection of either Aflibercept or Ranibizumab. Recruited candidates were examined for IOP and anterior segment biometry using Visante "anterior segment-optical coherence tomography" (AS-OCT) before and after injection. The anterior segment biometry measured in this study includes central anterior chamber depth, angle opening distance at nasal and temporal (AOD500 nasal, AOD500 temporal), and trabeculo-iris angle at nasal and temporal (TIA500 nasal and TIA500 temporal). **Results:** Mean (SD) increment of IOP following injection within 30 minutes and 1 hour were 6.16 (0.68) mmHg ($p<0.001$) and 1.26 (0.35) mmHg ($p=0.002$) respectively. Mean (SD) differences of TIA500 temporal between pre with within 30 minutes and 1-hour post-injection were 1.66 (0.66) degrees ($p=0.04$) and 1.45 (0.57) degrees ($p=0.04$) respectively. The changes of other anterior segment biometry parameters were not significant. Also, no significant relationship between IOP changes and anterior segment biometry was found. **Conclusions:** A single dose of intravitreal anti-VEGF injection is associated with short-term raised in IOP. There are no significant changes in anterior segment biometry parameter except for TIA500 temporal and it has no statistically significant relationship with IOP changes post intravitreal anti-VEGF.

Keywords
Intraocular pressure, anterior segment biometry, anti-VEGF

3.3 Introduction

Intravitreal injection of anti-vascular endothelial growth factors (anti-VEGF) is getting more and more popular nowadays (1). In United States, several million anti-VEGF injections are administered every year and this number is still increasing each year (2). Placental growth factor (PLGF), VEGF A, VEGF B, VEGF C, VEGF D, and VEGF E are the six proteins described in the family of vascular endothelial growth factor (VEGF) (3), and these VEGF factors are believed to have a vital role in the progression of age-related macular degeneration as well other aetiologies of choroidal neovascularisation such as retinal vein occlusion, pathological myopia, and uveitis (4, 5). Thus, inhibiting the activity of VEGF is believed to be able to control the progression of neovascularisation in age-related macular degeneration (AMD). The available anti-VEGF agents for medical use are pegaptanib, bevacizumab, ranibizumab and aflibercept (4).

Meanwhile, several ocular and systemic complications following intravitreal injection of anti-VEGF are reported so far, of which the increase in intraocular pressure was found to be one of the most common confounding ocular complications. The other ocular complications such as infectious uveitis, retinal detachment, and subretinal haemorrhage also been reported (6).

Intraocular pressure (IOP) is defined as the fluid pressure within the eyes and it can be measured by the force applied by the aqueous fluid on the cornea. Theoretically, IOP is explained by Goldmann equation, in which IOP equal to [F (aqueous flow rate) / C (aqueous outflow)] + P (episcleral venous pressure). Meaning that, IOP will be altered by any fluctuation on these variables (7). Nevertheless, other ocular biometry such as the anterior chamber depth also influences the IOP (8).

Sudden rise of IOP would almost inevitably cause variable degree of mechanical injury and ischemic stress on the retinal nerve fiber layer (RNFL) if left untreated (7) , and this explained the main pathogenesis of progressive irreversible glaucoma especially in those with chronic elevation of IOP. Besides, the increase of oxidative stress and chronic inflammation have also been demonstrated in ocular hypertensive eye, which consequently causing irreversible tissue damage on retina and optic nerve (9). Even though only small volume of intravitreal anti-VEGF injection (which only 50µl) was given, immediate acute rise of high IOP post-injection has been reported, which contribute to acute symptoms of ocular pain and vision loss (10, 11).

Unfortunately, only limited studies available on anterior segment biometry following intravitreal injection of anti-VEGF, particularly on aflibercept or ranibizumab, and mainly involving Caucasians population. Also, variable ocular biometric parameters were reported between Caucasians and Asians, where greater angle recess area, anterior chamber width, iris curvature and thickness were found among Caucasians as compared to Chinese population (12). Only limited studies were conducted on the perspective of biometry changes in Asian countries and unfortunately non was conducted in Malaysia up to date. Furthermore, variable baseline IOP was identified among different ethnicity as well, of which Chua J et al from Singapore reported of mean IOP of 14.3±3.1 mmHg, 15.3±3.7 mmHg, and 15.8±2.9 mmHg among the Chinese, Malay, and Indian participants respectively (12).

This urge for local studies for better understanding regarding the anterior segment biometry changes and risk of developing high IOP following intravitreal injection of anti-VEGF among our local multiracial population. Besides, we would like to determine the relationship between the anterior segment biometry changes with the changes of IOP post intravitreal injection. With this study, we hope the outcome could alert our clinician on the spike of IOP

post anti-VEGF injection, and further guide the clinician's decision on prescribing IOP lowering drug pre- or post-intravitreal injection of anti-VEGF in order to prevent acute angle-closure attack especially among at-risk population.

3.4 Materials and Methods

This is a prospective cohort study conducted in Hospital Raja Permaisuri Bainun (HRPB) Perak, Malaysia from May 2020 to May 2021. Ethical approval was achieved from the research ethics committee of the School of Medical Sciences, Universiti Sains Malaysia [USM/JEPeM/20020102] and the National Medical Research Register [NMRR-19-3940-50159] in accordance with the Helsinki Declaration on Human Research. The study sample size was calculated using G Power 3.1, with a minimum sample of 72 subjects required.

At Hospital Raja Permaisuri Bainun Ipoh, patients who required intravitreal treatment of anti-VEGF injection for various pathology will be scheduled as daycare procedure at appointed date. Those potential subjects who fulfilled both the inclusion, and exclusion criteria for the study were identified during pre-procedure screening and were invited to join the research. The inclusion criteria include patients of age more than 17 years old who receiving the first dose of intravitreal anti-VEGF. On the other hand, patients with underlying glaucoma, glaucoma suspect, ocular hypertension, or intumescence cataract, history of intraocular surgery or ocular trauma, and refractive error with more than +/-4D were excluded from the study.

After the recruitment of subjects, potential patients were invited to consultation room, and the purpose of the study, participants criteria, study procedures, risk of participation, and safety assessment of the study were explained. Written detailed information was provided to the selected subjects, and written consents were taken from those consented.