EVALUATION OF OCULAR BIOMETRY PARAMETERS BEFORE AND AFTER INSTILLATION OF TROPICAMIDE 1.0%, PHENYLEPHRINE 2.5% AND COMBINATION OF TROPICAMIDE 1.0% - PHENYLEPHRINE 2.5% EYE DROPS

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ABSTRAK:

Pengenalan:

Pengukuran yang tepat dalam kuasa kanta intraokular memainkan peranan penting dalam mendapatkan kuasa kanta yang betul selepas pembedahan katarak. Dengan ini, ketepatan dalam pengukuran parameter biometri okular sebelum pembedahan adalah penting untuk mendapatkan kuasa kanta yang diinginkan bagi mengelakan kejutan refraktif selepas pembedahan. Ubat dilatasi mata seperti 'tropicamide' dan 'phenylephrine' telah digunakan secara meluas untuk pengembangan anak mata semasa pemeriksaan dan rawatan okular. Kesan mydriatik daripada ubat dilatasi mata akan menjejaskan pengukuran parameter biometri okular dan hasil akhir refraktif.

Objektif:

Objektif kami adalah untuk membandingkan perbezaan dalam parameter biometri okular sebelum dan selepas pengembangan anak mata dengan penggunaan ubat dilatasi mata. Kajian ini juga untuk membandingkan tahap purata perbezaan untuk parameter biometri okular selepas pengembangan anak mata antara kumpulan yang berbeza.

Kaedah:

Kajian percubaan rawak terkawal telah dijalankan dari Disember 2015 hingga Disember 2017 di dua klinik mata hospital tertiari di Malaysia; iaitu Hospital Universiti Sains Malaysia dan Hospital Raja Permaisuri Bainun Ipoh. Bacaan parameter biometri okular ("axial length", "keratometry readings" dan "anterior chamber depth") diambilkan dengan menggunakan mesin "IOL Master" sebelum dan selepas ubat dilatasi mata. Analisis statistik dilakukan dengan menggunakan Pakej Statistik untuk Sains Sosial (SPSS Inc Versi 22).

Keputusan:

Seramai 321 pesakit [kumpulan 1 ("Tropicamide 1%"): 107 pesakit, kumpulan 2 ("Phenylephrine 2.5%"): 107 pesakit, kumpulan 3 (Kombinasi "Tropicamide 1% - Phenylephrine 2.5%"): 107 pesakit] telah terlibat dalam kajian ini. Dalam kumpulan 1, "mean keratometry reading" (P=0.028), "keratometry 2 reading" (P=0.028) dan "anterior chamber depth" (P<0.001) didapati ada perbezaan yang signifikan selepas pengembangan anak mata. Manakala dalam kumpulan 2, perbezaan yang signifikan didapati pada "mean keratometry reading" (P=0.003), "keratometry 2 reading" (P=0.002), "keratometry 1 and 2 axis" (P=0.010) dan "anterior chamber depth" (P<0.001) selepas pengembangan anak mata. Dalam kumpulan 3, "mean keratometry reading" (P<0.001), "keratometry 2 reading" (P<0.001), "keratometry 1 axis " (P=0.008) dan "keratometry 2 axis" (P=0.006), "astigmatism power" (P<0.001) dan "anterior chamber depth" (P<0.001) didapati mempunyai signifikasi perbezaan selepas pengembangan anak mata.

Semasa membandingkan perbezaan antara kumpulan-kumpulan, didapati bahawa perbezaan yang signifikan bagi purata perbezaan untuk "keratometry 2 reading" antara kumpulan 1 dan 3 [-0.049 (SD=0.228) diopters vs -0.143 (SD=0.195) diopters, P=0.004], kumpulan 2 dan 3 [-0.036 (SD=0.207) diopters vs -0.143 (SD=0.195) diopters, P=0.017]. "Keratometry 1 axis" antara kumpulan 1 dan 3 [1.065 (SD=11.252) ° vs -3.319 (SD=12.605) °, P=0.010] dan "keratometry 2 axis" antara kumpulan 1 dan 3 [1.075 (SD=11.252) ° vs -3.383 (SD=12.576) °, P=0.008] juga menunjukkan perbezaan yang signifikan. Sementara itu, purata perbezaan untuk "anterior chamber depth" juga menunjukkan perbezaan yang signifikan di antara kumpulan 1 dan 2 [-0.155 (SD=0.170) mm vs -0.070 (SD=0.086) mm, P=0.032], kumpulan 2 dan 3 [-0.070 (SD=0.086) mm vs -0.127 (SD=0.108) mm, P=0.003].

Kesimpulan:

Kajian ini menunjukkan bahawa terdapat perbezaan yang signifikan dalam "mean keratometry reading", "keratometry 2 reading" dan "anterior chamber depth" selepas pengembangan anak mata dalam ketiga-tiga kumpulan ini. Manakala "keratometry 1 and 2 axis" didapati mempunyai perbezaan yang signifikan dalam kumpulan 2 dan 3. "Astigmatism power" pula mempunyai kesan yang signifikan dalam kumpulan 3 sahaja. Purata perbezaan untuk "keratometry 2 reading", "keratometry 1 and 2 axis" dan "ACD" dalam kumpulan 3 didapati lebih tinggi jika dibandingkan dengan dua kumpulan yang lain. Kebanyakan parameter biometri okular dalam ketiga-tiga kumpulan ini telah mengalami perubahan kerana proses pengembangan anak mata dan kesannya lebih ketara dalam kumpulan 3. Daripada kajian yang dijalankan ini, kami

berpendapat bahawa pengukuran parameter biometri okular tidak boleh dilakukan selepas pengembangan anak mata, terutamanya dengan penggunaan kombinasi "tropicamide 1% and phenyephrine 2.5%". Ini adalah untuk mengelakkan kejutan refraktif selepas pembedahan katarak dan untuk medapatkan kuasa kanta yang lebih tepat, terutamanya untuk pembetulan "astigmatism power" dan "axis" dalam "toric lens".

ABSTRACT

Introduction:

The correct calculation of intra-ocular lens power is important for obtaining a high accuracy of postoperative refractive status. With that, the accuracy of the measurement of preoperative ocular biometry parameters (axial length, keratometry readings and anterior chamber depth) are important to obtain a precise IOL power to avoid postoperative refractive surprise. Topical dilating drops such as tropicamide and phenylephrine are widely used for pupil dilatation during an ocular examination and treatment. The mydriatic effect of the dilating eye drops might affect the ocular biometric parameters data which then can affect the final refractive outcome.

Objective:

The aim of our study was to evaluate the change in ocular biometry parameters before and after administration of tropicamide 1.0%, phenylephrine 2.5% and combination of tropicamide 1.0%-phenylephrine 2.5% eye drops. The secondary aim was to compare the mean difference of ocular biometry parameters between the groups.

Methods:

A randomised controlled trial study was conducted at Ophthalmology clinic, Hospital Universiti Sains Malaysia and Hospital Raja Permaisuri Bainun Ipoh from December 2015 to December 2017. The ocular biometric parameters (axial length, keratometric readings, anterior chamber depth) were obtained using noncontact partial coherence interferometer (IOL Master, Carl Zeiss, Germany) before and after the instillation of the dilating eye drops. Statistical analysis was done using Statistical Package for the Social Science, Version 22.

Results:

A total of 321 patients [group `1 (Tropicamide 1.0%): 107 patients, group 2 (Phenylephrine 2.5%): 107 patients, group 3 (Combination of Tropicamide 1% - Phenylephrine 2.5%): 107 patients] were recruited into this study. In group 1, the mean keratometry reading (P=0.028), keratometry 2 reading (P=0.028) and anterior chamber depth (P<0.001) were significantly different following pupil dilatation. In group 2, the mean keratometry reading (P=0.003), keratometry 2 reading (P=0.002), keratometry 1 and 2 axis (P=0.010) and anterior chamber depth (P<0.001) were significantly different between pre and post pupil dilatation. In group 3, the mean keratometry reading (P<0.001), keratometry 2 reading (P<0.001), keratometry 1 (P=0.008) and 2 axis (P=0.006), astigmatism power (P<0.001) and anterior chamber depth (P<0.001) were significantly different post pupil dilatation. Comparisons between the groups revealed statistically significant differences in the mean difference of keratometry 2 reading between group 1 and 3 [-0.049 (SD=0.228) diopters vs -0.143 (SD=0.195) diopters, P=0.004],

group 2 and 3 [-0.036 (SD=0.207) diopters vs -0.143 (SD=0.195) diopters, P=0.017]. The keratometry 1 axis between group 1 and group 3 [1.065 (SD=11.252) ° vs -3.319 (SD=12.605) °, P=0.010] and keratometry 2 axis between group 1 and group 3 [1.075 (SD=11.252) ° vs -3.383 (SD=12.576) °, P=0.008] also showed statistically significant results. Meanwhile, the mean difference of anterior chamber depth also showed statistically significant difference between group 1 and 2 [-0.155 (SD=0.170) mm vs -0.070 (SD=0.086) mm, P=0.032], group 2 and 3 [-0.070 (SD=0.086) mm vs -0.127 (SD=0.108) mm, P=0.003] respectively.

Conclusion:

This study showed that the mean keratometry, keratometry 2 reading and anterior chamber depth were significantly different post pupil dilation in all three groups. Meanwhile the keratometry 1 and 2 axis were statistically significant different in group 2 and 3. The astigmatism power was significantly affected in group 3 only. The mean difference of keratometry 2 reading, keratometry 1 and 2 axis and anterior chamber depth in group 3 were significantly higher compared to the other two groups. Most of the ocular biometry parameters were significantly affected post pupil dilation, and especially in group 3. We suggest to defer measuring the ocular biometry parameters after pupil dilation, especially after instillation of combined tropicamide 1% and phenylephrine 2.5% eye drops. This is to avoid the unexpected refractive surprise post cataract surgery and to obtain the most accurate postoperative refractive status, especially for the precise correction of the astigmatism power and axis in toric lens.

CHAPTER 1

INTRODUCTION

1.1 Prevalence of Cataract:

Cataract is the leading cause of blindness worldwide. The global prevalence of blindness due to cataract is 33.4% (Khairallah *et al.*, 2015; Pascolini and Mariotti, 2012). The main causes of visual impairment globally are contributed by refractive errors and then followed by cataracts (Pascolini and Mariotti, 2012).

The Malaysia National Eye Survey 1996 provided important epidemiological data regarding the causes and prevalence of low vision and blindness in Malaysia. The survey findings showed that uncorrected refractive errors and cataract were the main causes of visual impairment in the Malaysian population. For the causes of blindness, cataract was noted to be the major cause of bilateral blindness and then followed by retinal diseases. Other than this, the major cause of low vision was uncorrected refractive errors and then followed by cataract (Zainal *et al.*, 2002). With that, cataract surgery is the main treatment for cataract to settle the problem of blindness worldwide.

The 8th report of the National Eye Database 2014 showed that the total number of registered cataract surgeries in National Cataract Surgery Registry increased from 18426 in year 2007 to 40532 in year 2014 from 43 participating centres in Malaysia (Mohamad *et al.*, 2016). A good outcome of cataract surgery with accurate postoperative visual refraction therefore serves as an indicator of a good quality of eye surgery ("Ministry of health Malaysia", 2004).

1.2 Ocular Biometry Parameters used in Intra-ocular Lens Calculation:

The correct calculation of intra-ocular lens (IOL) power is important to obtain a high accuracy of postoperative refractive status. The accuracy of the measurement of preoperative ocular biometry parameters and the use of proper biometry formulas are essential for obtaining a precise IOL power. The ocular biometry parameters involved in the calculation of IOL power including axial length (AL), keratometric power and anterior chamber depth (ACD) (Wang and Chang, 2013). Various IOL formulas are used, such as the 3rd generation formulas, Holladay 1, Hoffer Q and SRK/T, which are designed specifically to obtain a precise intraocular power that involves measurements of the biometry of the eye balls, including the AL and corneal curvatures (Butcher and O'Brien, 1991; Hsieh and Wang, 2012; Kim et al., 2009; Miraftab et al., 2014; Norrby, 2008a; Rajan et al., 2002).

The SRK formula is depend on the relationship between the preoperative ocular biometry variables including keratometric reading and AL, to obtain the implant power that provides post operative emmetropia.

The SRK formula is $P = A - 2.5\,AL - 0.9\,K$,

where P = implant power (dioptres) to achieve emmetropia;

 AL = axial length (mm);

 K = average keratometer reading (dioptres);

 A = specific constant for each lens type and manufacturer

(Adapted from factors affecting the predictability of SRK II in patients with normal axial length undergoing phacoemulsification surgery by Lim et al, 2009) (Lim et al., 2009)

The 4th generation formulas, such as Haigis formula and Olsen formula are one of the formulas which include an additional biometric parameter, preoperative ACD in IOL power calculation for the effective lens position prediction (Miraftab *et al.*, 2014; Olsen, 2007). Wang *et al* found that Haigis formula yielded better refractive outcomes in eyes with various AL compared to other biometry formulas by using IOL Master for ocular biometric measurement (Wang and Chang, 2013). Eom *et al* reported that the Haigis formula gave the best results when compared to Hoffer Q, Holladay I and SRK/T in their study. This is possibly due to its inclusion of measurement of ACD in the formula (Eom *et al.*, 2014). In view of this, the accuracy measurement of the ACD is important for the calculation of IOL power in 4th generation formulae such and Haigis and Olsen formula.

An error in the measurement of the ocular biometry parameters can lead to errors in IOL calculation. For example, every 1.0 mm error in AL measurement can lead to a 2.7 D error in IOL power calculation. A 1.0 mm error in corneal radius measurement can lead to a 5.7 D error in the IOL power calculation, while a 1.0 mm error in postoperative anterior chamber measurement can cause a 1.5 D error in the IOL power calculation (Olsen, 2007).

Variable	Error	Rx error
Corneal radius	1.0 mm	5.7 D
Axial length	1.0 mm	2.7 D
Postoperative ACD	1.0 mm	1.5 D
IOL power	1.0 D	0.67 D

Rx error = refraction error; ACD = anterior chamber depth; IOL = intraocular lens.

Table 1: Illustration shows the deviation from the mean values of different variables and its corresponding refraction error (Adapted from Calculation of Intraocular Lens Power: A Review by Olsen, 2007) (Olsen, 2007).

In a study by Jin *et al*, they found that the main factor for the incorrect IOL power insertion was an error in keratometry reading measurement which consisted of 23% and then followed by inaccurate AL measurement and a wrong IOL implantation (Jin *et al.*, 2007). However, Olsen *et al* found that the wrong AL measurement contributed to the main reason for the inaccurate intraocular lens calculation then followed by an error in postoperative ACD and corneal power measurement (Olsen, 1992).

There are a significant number of patients are noted to have corneal astigmatism before cataract surgery. Thus, the accurate and precise measurement of corneal power and axis preoperatively is also important for the calculation of accurate toric lens power to achieve the best postoperative visual acuity by correcting the corneal astigmatism and its axis (Chang *et al.*, 2012; Kessel *et al.*, 2016; Lee *et al.*, 2015; Mendicute *et al.*, 2008; Visser *et al.*, 2012). In addition, accurate measurement of corneal power is important for refractive surgery, contact lens fitting and orthokeratology also (Dehnavi *et al.*, 2015). Rotation of the toric IOL after implantation is the main problem associated with postoperative error in astigmatism power correction. One study has shown that the postoperative rotation of a toric IOL by approximately 1 degree can result in a loss of up to 3.3% of the lens cylinder power, while a rotation of the IOL by 30 degrees will lead to a complete loss of cylinder power (Mendicute *et al.*, 2008). Other studies have shown that a rotation of a toric IOL by 3 degrees reduces the compensatory effect by 10%, while a rotation of 11.5 degrees results in a 40% loss of its initial effect (Viestenz *et al.*, 2004).

1.3 IOL Master and Ocular Biometry Parameters Measurement:

Partial coherence interferometry (IOL Master, Zeiss Humphrey Systems) is a noncontact technique that uses the principle of partial coherence interferometry (PCI) compared to ultrasonography technique. PCI uses an infrared wave (590–880 nm) to measure the corneal convex to the retinal pigment epithelium layer and has a great resolution of up to 0.01 mm (Hussin *et al.*, 2005; Khambhiphant *et al.*, 2015b). The IOL Master is particularly convenient as it measures the AL, corneal radius and ACD in a single session. The corneal radius and ACD measurements are based on image analysis, while the AL measurement is based on the PCI principle.
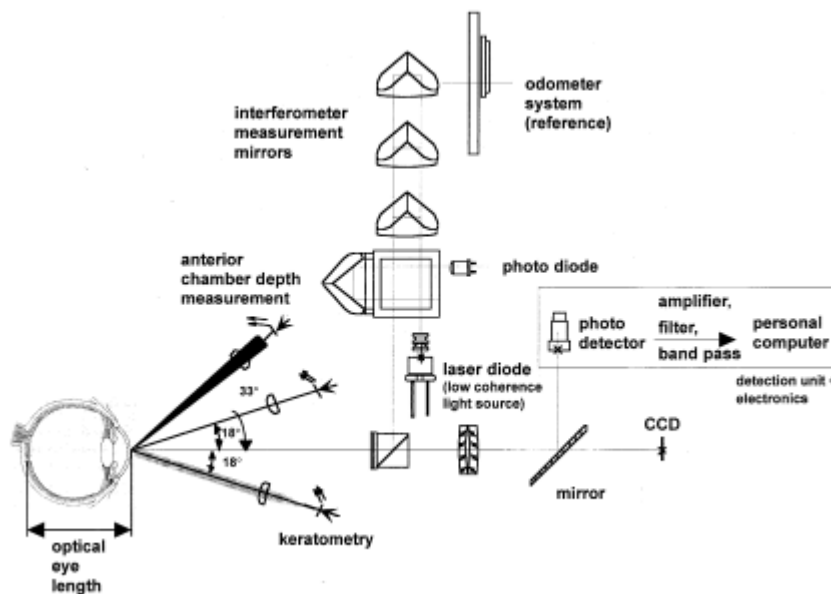

Figure 1: Illustration shows the measurement principle of the IOL Master.

The illustration shows a laser diode emits light, which will split into 2 parallel and coaxial beams of different optical path lengths in a Michelson interferometer (Figure 1). Both beams will go through a beam-splitting prism and will illuminate the eye. The light will be reflected

by the cornea and retina. A photo detector will detect the interference. An interferometer mirror will scan the eye longitudinally in which it will move across the measuring range during the measurement process. The signals are amplified, filtered, and recorded.

(Adapted from Reproducibility of Optical Biometry using Partial Coherence Interferometry by Vogel *et al*, 2002) (Vogel *et al.*, 2002)

With its feature of noncontact technique, PCI will reduce the risk of corneal injury and infection compared to applanation ultrasound technique. This is due to applanation ultrasound technique requires the immersion of the eye with saline solution or the eye contact by a transducer (Drexler *et al.*, 1998). Other than this, IOL Master is reported to be operator independent, precise, accurate and highly reproducible. It is also more efficient and comfortable for the patients (Findl *et al.*, 2003; Haigis *et al.*, 2000; Hussin *et al.*, 2005; Kiss *et al.*, 2002; Vogel *et al.*, 2002). It was found to be yielded significantly better IOL power prediction and improves the refractive outcomes (Eleftheriadis, 2003).

1.4.1 The action of Phenylephrine Hydrochloride

The phenylephrine hydrochloride is a selective α-adrenergic receptor agonist. It is used for decongestant and to increase blood pressure. It is also used in the form of topical eye drops and as a mydriatic agent to dilate the iris before ocular examination or ocular operation. It is expected to produce pupil dilation with no or little influence in the accommodation as it is a purely α-adrenoceptors agonist and has minimal influence on the β-adrenoceptors in ciliary muscle (Esteve-Taboada *et al.*, 2016; Lin *et al.*, 2013). In human ciliary muscle, there are more β than α-adrenoceptors. So it is possible that phenylephrine may act on α receptors in

the ciliary muscle also and alter the ciliary muscle. However, Richdale *et al* found that topical phenylephrine 2.5% does not affect ciliary muscle contractile or dimensions and accommodative effect in their study (Richdale *et al.*, 2012). The phenylephrine 2.5% is usually used for fundus examination and 10% concentration is usually used to break the pupillary block and posterior synechiae therapeutically. It causes mydriasis in 15 to 30 minutes, and the effect lasts for one to three hours duration. Its side effects include hypertension as a result of systemic hypertension and local irritation (Lam *et al.*, 2010)

1.4.2 The Action of Tropicamide

Tropicamide is an acetylcholine receptor antagonist (antimuscarinic agent). It has short acting cycloplegic and mydriatic effect (Bhatia, 2011). It causes mydriasis within 20 minutes and the cycloplegic effects within 20 to 30 minutes and it lasts for 6 hours prior to recovery of the accommodation (Lam *et al.*, 2010; Yazdani *et al.*, 2017). Its side effects divided into ocular and systemic side effects. The ocular side effects include corneal irritation, stinging sensation, raise in intraocular pressure. Then, the systemic side effects include flushing, dry mucous membranes and tachycardia (Yazdani *et al.*, 2017).

1.5.1 The measurement of the keratometry readings and the effect of the mydriasis and miosis on corneal curvature:

The IOL Master measures the anterior corneal curvature by using the automated keratometry. Six spots of light are projected within a 2.3 mm area onto the cornea in a hexagonal pattern. The anterior radium of curvature (mm) is converted into a corneal power (diopters) by using

a refractive index of 1.3375 (Visser *et al.*, 2012). Three separate measurements were recorded for corneal curvature in each session of measurement.
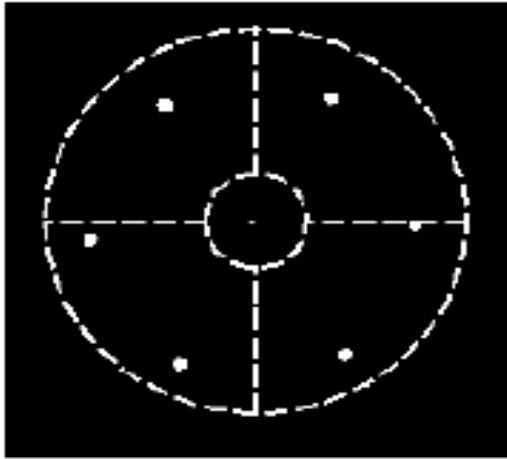

Figure 1: Illustration demonstrates 6 peripheral circular points are visible and located in between the two auxiliary circles on the display.

(Adapted from The Repeatability and Accuracy of Axial Length and Anterior Chamber Depth Measurements from the IOLMaster by Lam *et al*, 2001) (Lam *et al.*, 2001)

Previous studies have reported on the changes in corneal curvature after mydriasis or miosis effect. Saitoh *et al* found that there was change in the anterior and posterior corneal shapes due to the mydriasis and miosis effect in their study. They noted that sympathomimetic agent had causing the mydriasis by relaxing the ciliary muscle and then corneal flattening. While the parasympathomimetic agent had causing the miosis effect by contracting the ciliary muscle and its force will act on the peripheral cornea through the sclera spur in which it will lead to corneal steepening (Saitoh *et al.*, 2004). Besides this, a study conducted by Heatley *et al* to investigate the effect of pupil dilation on the accuracy of the IOL Master and their result showed that there was statistically significant change in keratometry reading 2 and

average keratometry values in their study (Heatley *et al.*, 2002). There was also another study showed that the keratometry 1 was statistically significant difference post pupil dilation. But there was no significant changes in keratometry 2, average keratometry and astigmatism power (Bakbak *et al.*, 2013).

However, a study was conducted by Huang *et al* and they investigated the effect of mydriasis from phenylephrine on corneal shape. They found that there was no significant corneal shape alteration and it cause minimal effect on accommodation due to the mydriasis effect from phenylephrine (Huang and Lam, 2007). Daily *et al* conducted a study to determine the effect of anesthetic and mydriatic drops on the cornea curvature and they found that there was no significant change on the cornea shape after the application of the anesthetic and cycloplegic eye drops (Daily and Coe, 1962). Besides this, there was a study found that the instillation of the ophthalmic solutions such as topical anaesthetic, mydriacyl, fluorescein and contact lens wetting solutions also did not cause the corneal contour alteration or alter the corneal topography (Kiely and Carney, 1978).

There was numerous other studies have shown that the pupil dilation did not cause a significant effect on keratometry readings or corneal curvature (Arriola-Villalobos *et al.*, 2014; Huang *et al.*, 2012; Khambhiphant *et al.*, 2015a; Rodriguez-Raton *et al.*, 2015). From the previous literatures review, we found that the finding of the changes in keratometry reading after pupil dilation was different between the few studies mentioned (Arriola-Villalobos *et al.*, 2014; Bakbak *et al.*, 2013; Heatley *et al.*, 2002; Huang *et al.*, 2012; Khambhiphant *et al.*, 2015a; Rodriguez-Raton *et al.*, 2015; Saitoh *et al.*, 2004).

1.5.2   The effect of accommodation on corneal shape

Accommodation is associated with the dynamic focusing process due to the change in the shape of the crystalline lens which is contributed by the ciliary muscle action (Pierscionek *et al.*, 2001). The ciliary muscle movement could apply slight effect over the lens and the force will extend into the cornea through the anterior sclera in which it contacts with the ciliary muscle fibers. Pierscionek *et al* found that there may have some influence on the corneal shape with accommodation. There was a difference of about 0.4 dioptres in at least one of the principle meridian in the central corneal curvature during accommodation (Pierścionek *et al.*, 2001).

There was few studies found that the accommodation process was associated with changes in corneal curvature with a steepened corneal curvature during accommodation process (Yasuda *et al.*, 2003, He *et al.*, 2003). However, Buehren *et al* found that there was no statistically significant changes in cornea shape for the normal and keratoconic corneas due to the accommodation (Buehren *et al.*, 2003).

1.5.3 The effect of mydriasis in anterior chamber depth measurement:

The ACD is the measurement from the anterior surface of the cornea to the anterior surface of the crystalline lens (Patel and Pandit, 2012). For the measurement of ACD, it is using the technique of image analysis. A 0.7 mm-wide slit beam of light is directed to the visual axis through the anterior chamber at a 30 degrees angle. It measures the distance of the light reflection between the anterior surface of the cornea and the anterior surface of crystalline

lens. A serial of 5 measurements are taken and the average of it will be calculated (Elbaz *et al.*, 2007).
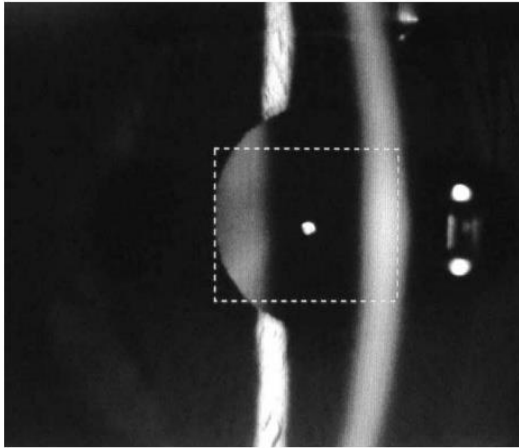

Figure 2: Illustration demonstrates the correct alignment with the fixation point in between the images of the cornea and the crystalline lens, and lies within the square. (Adapted from The Repeatability and Accuracy of Axial Length and Anterior Chamber Depth Measurements from the IOL Master by Lam *et al*, 2001) (Lam *et al.*, 2001)

The Haigis formula uses a measured ACD, three IOL and surgeon-specific constants (a0, a1 and a2) to determine the shape and position of the IOL power prediction curve. In this formula, the measurement of the corneal power is not needed. Thus, the errors in the prediction of postoperative effective lens position and the measurement of the anterior corneal power are avoided with this formula (Lee *et al.*, 2008).

The following regression is used for the ACD prediction in Haigis formula:

ACD = a_0 + a_1 * C + a_2 * A

Where a_0 = constant closely related to the ACD constant,

   a1 = regression coefficient for the preoperative anterior chamber depth C,

   a2 = regression coefficient for the preoperative axial length A.

The default values of a1 and a2 were 0.4 and 0.1, respectively.

(Adapted from Prediction of the effective postoperative (intraocular lens) anterior chamber depth by *Olsen, 2006*) (Olsen, 2006)

The prediction and calculation of the postoperative effective lens position is depending on the accurate measurement of preoperative ACD in some of the formulas, such as Olsen formula. The ACD prediction of the Olsen formula incorporating AL, phakic ACD, cornea height and lens thickness (Olsen *et al.*, 1995):

ACDpost = ACDconst + 0.50*ACDpre + 0.10*A + 0.15*H + 0.20*L-5.38

Where ACDpost = estimated individual pseudophakic anterior chamber depth (distance from the corneal surface to the anterior surface of the lens);

   ACDconst = mean ACD (ACD constant) of the given cons IOL;

   ACDpre = phakic anterior chamber depth;

   A = axial length, H = corneal height, and L = lens thickness

(Adapted from Intraocular lens power calculation with an improved anterior chamber depth prediction algorithm by *Olsen et al, 1995*) (Olsen *et al.*, 1995)
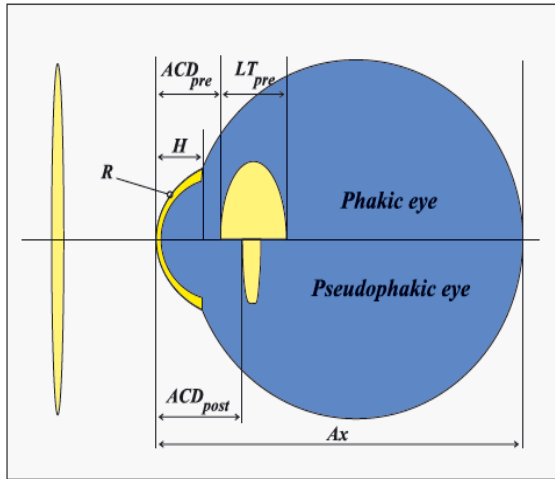
Figure 3: Illustration demonstrates prediction of postoperative anterior chamber depth (ACDpost), which is the distance from anterior cornea surface to anterior surface of Intra-ocular lens.

Ax: axial length; ACDpre: preoperative ACD; LT: lens thickness; R: front radius of cornea; H: cornea height

(Adapted from Calculation of intraocular lens power: a review by *Olsen, 2007*) (Olsen, 2007)

The accurate measurement of ACD is crucial for good postoperative refractive outcome with the use of Holladay 2, Haigis or Olsen formulas (Patel and Pandit, 2012). A precise ACD measurement is needed in order to determine IOL position and power. It is also important to prevent cornea endothelial cell injury during cataract surgery (Bhatia, 2011).

Norrby *et al* found that an error in ACD for every +/- 0.10 mm will lead to refractive error of +/- 0.14 D (Norrby, 2008). Numerous studies have shown that the ACD was significantly increased after pupil dilation with dilating drops (Arriola-Villalobos *et al.*, 2013; Arici *et al.*, 2014; Huang *et al.*, 2012; Khambhiphant *et al.*, 2015a; Rodriguez-Raton *et al.*, 2015; Saitoh *et al.*, 2004).

1.5.4 The effect of mydriasis in axial length measurement:

The AL is the distance from the anterior surface of the cornea and the retinal pigment epithelium (Drexler *et al.*, 1998; Haigis *et al.*, 2000). It uses the technique of PCI with an infrared diode laser with a wavelength of 780 nm for AL measurement. The measurement of AL with IOL Master is repeatable and accurate (Lam *et al.*, 2001).

AL measurement acquisition failure with the IOL Master has been reported in the literature. Causes have been attributed to an inability to position the patient at the instrument due to the head tremor, a combination of low vision and lens opacity, and fixation difficulties due to macular disease. Poor visual acuity and lens opacity appear to be the most common reported cause of failure in AL measurement (Tehrani *et al.*, 2003). Freeman *et al* also found that the posterior subcapsular cataract being the main reason in contributing the failure in AL measurement (Freeman and Pesudovs, 2005).
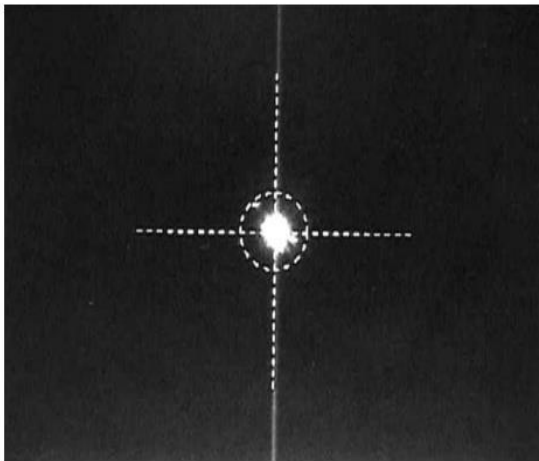
Figure 3: Illustration demonstrates the reflection of light and the vertical line is within the circle.

(Adapted from The Repeatability and Accuracy of Axial Length and Anterior Chamber Depth Measurements from the IOL Master by Lam *et al*, 2001) (Lam *et al.*, 2001)

Heatley *et al* found that there was no significant changes in AL after pupil dilation (Heatley *et al.*, 2002). There was also several studies showed that there was no significant effect on AL after pupil dilation (Arriola-Villalobos *et al.*, 2014; Huang *et al.*, 2012; Khambhiphant *et al.*, 2015a; Rodriguez-Raton *et al.*, 2015).

Rationale of the study

The correct calculation of IOL power is important to obtain a high accuracy of postoperative refractive outcome. The accuracy of the measurement of preoperative ocular biometric parameters such as AL, keratometric power and ACD with the use of proper biometry formulas are important to obtain and determine a precise IOL power (Olsen, 2007; Wang and Chang, 2013).

Topical dilating drops such as tropicamide and phenylephrine are widely used for pupil dilatation during ocular examination and treatment (Park *et al.*, 2009). Dilated pupils for lens and funduscopic examination are mandatory in most of the ophthalmic cases especially during preoperative assessment for cataract surgery. The cycloplegic effect of the dilating eye drops might affect the cornea curvature which would then influence the keratometric measurement (Bakbak *et al.*, 2013; Heatley *et al.*, 2002; Saitoh *et al.*, 2004). Besides this, it also can cause the changes in the shape of the lens and then might affect the ACD. Previous studies evaluating the effect of dilating drops on the ocular biometric parameters have reported conflicting results on the keratometric power readings. Saitoh *et al*, Heatley *et al* and Bakbak *et al* noted that the keratometric power readings were significantly different post pupil dilation (Bakbak *et al.*, 2013; Heatley *et al.*, 2002; Saitoh *et al.*, 2004) compared to other studies which did not show any significant changes in the keratometric power post pupil dilation (Arriola-Villalobos *et al.*, 2014; Huang *et al.*, 2012; Khambhiphant *et al.*, 2015a; Khambhiphant *et al.*, 2016; Rodriguez-Raton *et al.*, 2015).

Apart from this, the accurate keratometric data including the power and axis are especially important for the toric lens calculation in order to correct the pre-existing astigmatism effectively in a cataract surgery (Kessel *et al.*, 2016; Lee *et al.*, 2015; Mendicute *et al.*, 2008; Visser *et al.*, 2012). Inaccuracy in keratometric power and axis measurements may cause worsening in the corneal astigmatism power (Chang *et al.*, 2012). The precise measurement of astigmatism power and axis are particularly crucial to avoid in the postoperative refractive error. However, there was relatively lack of studies on the changes in keratometric axis or astigmatism axis after instillation of dilating drops.

The previous studies also found that there were significant changes in ACD post pupil dilation and the ACD is essentially important for the IOL power calculation with some of the formulas such as Haigis and Olsen formulas (Arriola-Villalobos *et al.*, 2013; Arici *et al.*, 2014; Huang *et al.*, 2012; Khambhiphant *et al.*, 2015a; Rodriguez-Raton *et al.*, 2015; Saitoh *et al.*, 2004).

In view of the topical dilating drops, especially those with cycloplegic effect can affect the final ocular biometric parameters measurement and then the post operative refractive outcome. And those without cycloplegic effect such as phenylephrine with minimal or no effect on the accommodation may affect the cornea curvature and ACD. To date, data on the changes in ocular biometry parameters after pupil dilation in Asian population are very limited and so far no study has been done to compare the mean difference of ocular biometric parameters between the different types of dilating drops. The aim of our study was to evaluate the changes in ocular biometry parameters before and after administration of tropicamide 1.0%, phenylephrine 2.5% and combination of tropicamide 1.0%-phenylephrine

2.5% eye drops. The secondary aim was to compare the mean difference of ocular biometry parameters before and after pupil dilation between the different types of dilating drops. By determining the effects of pupillary dilation on ocular biometry parameters, the incidence of wrong intra-ocular lens power calculation can be minimized to reduce poor refractive outcomes post cataract surgery. If this study shows that there is no significant effect on ocular biometry parameters measurement after pupil dilation, ocular biometry parameters can be measured on the same day of ocular examination. It can reduce one clinic visit for ocular biometry measurement for the purpose of IOL power calculation prior to operation. This is of practical significant to both the physician and patients as it can reduce the number of clinic visits and hasten the preoperative assessment process.

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