THE RELATIONSHIP OF LENS THICKNESS AND ANTERIOR CHAMBER DEPTH WITH INTRAOCULAR PRESSURE DURING HEMODIALYSIS

By

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ABSTRAK

Pengenalan: Hemodialisis merupakan rawatan penggantian ginjal terhadap kegagalan ginjal peringkat terakhir. Perubahan tekanan mata berlaku semasa hemodialisis. Seseorang yang ada masalah pengaliran akueous lebih berisiko mendapat gejala kenaikan tekanan mata. Perubahan ketebalan kanta boleh mengakibatkan perubahan kedalaman ruang depan mata yang boleh memudaratkan lagi masalah pengaliran akueous. Pengesanan awal perubahan kanta semasa hemodialisis dapat mencegah kenaikan tekanan mata dan kebutaan. Oleh demikian, penilaian perubahan ketebalan kanta dan kedalaman ruang depan mata dengan tekanan mata semasa hemodialisis adalah penting.

Objektif: Untuk menentukan min ketebalan kanta dan hubungan di antara ketebalan kanta dan kedalaman ruang depan mata, antara kedalaman ruang depan mata dan tekanan mata serta antara ketebalan kanta dan tekanan mata semasa hemodialisis.

Tatacara: 70 mata dari 70 peserta kajian yang dipilih dari Unit Hemodialisis, Hospital Queen Elizabeth. Ketebalan kanta, kedalaman ruang depan mata dan tekanan mata diukur pada 0 jam, 2 jam dan 4 jam hemodialisis. Perubahan ketebalan kanta, kedalaman ruang depan mata dan tekanan mata berdasarkan masa hemodialisis dikaji dengan ujian statistik ‘repeated measures ANCOVA’ dan ‘multiple paired samples T-test’ dengan ‘bonferonni correction’(p=0.017). Hubungan di antara parameter kajian ditentukan dengan ‘correlation analysis’.

Keputusan: Kajian menunjukan peningkatan ketebalan kanta dan tekanan mata yang signifikan untuk keseluruhan peserta kajian sebanyak 0.21 ± 0.69 mm (p=0.015) dan 1.26 ± 3.02mmHg (p=0.001) dalam masa 2 jam yang pertama hemodialisis. Perubahan kedalaman ruang depan mata adalah tidak signifikan. Peningkatan min ketebalan kanta dan tekanan mata adalah lebih ketara dalam kumpulan diabetik dan umur tua dalam masa 2 jam yang pertama hemodialisis tetapi hanya perubahan tekanan mata adalah signifikan. Pada jam ke-2 hemodialisis, ia menunjukan hubungan songsang di antara ketebalan kanta dan kedalaman ruang depan mata, hubungan songsang di antara kedalaman ruang depan mata dan tekanan mata serta hubungan linear di antara ketebalan kanta dan tekanan mata tetapi tidak signifikan. Pada jam ke-4 hemodialisis, ia menunjukan hubungan songsang yang memuaskan dan signifikan di antara ketebalan kanta dan kedalaman ruang depan mata (r = -0.286, p=0.016) tetapi hubungan parameter yang lain adalah tidak signifikan.

Kesimpulan: Dalam masa 2 jam pertama hemodialisis, peningkatan ketebalan kanta dan tekanan mata adalah signifikan tetapi hubungan di antara parameter kajian adalah tidak signifikan mencadangkan mekanisma kenaikan tekanan mata adalah bukan disebabkan oleh ketebalan kanta sahaja. Hubungan songsang yang signifikan di antara ketebalan kanta dan kedalaman ruang depan mata terjadi pada jam ke-4 hemodialisis tetapi ia tidak menyebabkan kenaikan tekanan yang signifikan di dalam mata yang normal. Kenaikan tekanan mata boleh menjadi signifikan sekiranya seseorang mempunyai mata yang bermasalah pengaliran akueous. Diabetes mellitus dan umur mempunyai kesan yang signifikan pada tekanan mata tetapi tiada kesan signifikan pada ketebalan kanta dan kedalaman ruang depan mata semasa hemodialisis.

ABSTRACT

Introduction: Hemodialysis is a common renal replacement therapy in the end stage renal failure. Fluctuation of intraocular pressure occurred during hemodialysis. Individuals with compromised aqueous outflow facility have increased risk of symptomatic elevation of intraocular pressure. Lens thickness changes may result in alteration of anterior chamber depth that can further compromise aqueous drainage. Early detection of the lens thickness changes during hemodialysis can prevent elevation of intraocular pressure and visual loss. Thus, evaluation of the lens thickness and anterior chamber depth with intraocular pressure changes during hemodialysis are essential.

Objectives: To determine the mean lens thickness and the relationship between lens thickness and anterior chamber depth, between anterior chamber depth and intraocular pressure as well as between lens thickness and intraocular pressure during hemodialysis.

Methodology: 70 eyes from 70 study subjects were recruited from Hemodialysis Unit, Queen Elizabeth Hospital. Lens thickness, anterior chamber depth and intraocular pressure were measured at 0hour, 2hour and 4hour of hemodialysis. The mean lens thickness, anterior chamber depth and intraocular pressure changes based on time effect of hemodialysis were analyzed with repeated measures ANCOVA and multiple paired samples T-test with bonferonni correction ($p=0.017$). The relationship between study variables were evaluated with correlation analysis.

Results: There were significant increased mean lens thickness and intraocular pressure among all study subjects by 0.21 ± 0.69 mm (p=0.015) and 1.26 ± 3.02mmHg (p=0.001) in the first 2hours of hemodialysis. The anterior chamber depth changes was insignificant. The mean lens thickness and intraocular pressure were increased more in diabetic and older age group in the first 2hours of hemodialysis but significant for intraocular pressure changes only. At 2hours of hemodialysis, there were inverse correlation between lens thickness and anterior chamber depth, inverse correlation between anterior chamber and intraocular pressure, and linear correlation between lens thickness and intraocular pressure but not significant. At 4hour of hemodialysis, there was a significant fair inverse correlation between lens thickness and anterior chamber depth (r = -0.286, p=0.016) but the correlation between other variables were not significant.

Conclusions: In the first 2hours of hemodialysis, there were significant increased mean lens thickness and intraocular pressure but no significant correlation between study variables suggested other mechanisms of raised intraocular pressure were involved rather than due to lens thickness changes only. A significant inverse relationship between lens thickness and anterior chamber depth was established at 4hours of hemodialysis but it didn't lead to significant raised intraocular pressure in normal eyes. Intraocular pressure rise may become significant if individuals have compromised aqueous drainage. Diabetes mellitus and age had significant influence on intraocular pressure but not on lens thickness and anterior chamber depth during hemodialysis.

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1.1 BACKGROUND OF THE STUDY

Chronic kidney disease is a disease that occurs gradually, over months to years, with loss of the renal function over time. Chronic kidney disease is divided into 5 stages of increasing severity based on the glomerular filtration rate (GFR). GFR is the standard means of expressing overall renal function. Normal GFR is 100-140ml/min in men and 85-115ml/min in women. GFR decreases with age and it falls with the progress of kidney diseases. Stage 5 chronic kidney is referred as end stage renal failure. The GFR of this stage 5 CKD is less than 15ml/min/1.73m^2. At this stage , there is total or near total loss of the kidney function. Complication of end stage renal failure such as accumulation of water, waste products and toxic substances in the body, anemia, high blood pressure, metabolic acidosis, and bone disease. At this stage, most individuals need renal replacement therapy. (Eknoyan G, 2002).

Center of disease control of United States reported that the prevalence of chronic kidney disease was increased. There were 16.8% of the United States , population aged more than 20 years old had chronic kidney disease in 1999 to 2004 data compared to 14.5% in 1988 to 1994 data. Individuals with cardiovascular disease and diabetes mellitus had greatest risk of chronic kidney disease. Age group more than 60 years old (39.4%) was more prevalent than others. They also reported that the non-Hispanic blacks (19.9%) and Mexican America (18.7%) were more prevalent than non-Hispanic whites (16.1%) (Saydah *et al*., 2007).

The major causes of chronic kidney disease are diabetes mellitus and hypertension. Other causes of chronic kidney disease are glomerulonephritis (post infection and systemic lupus erythematosus), polycystic kidney disease, analgesic (acetaminophen and ibuprofen), and obstructive nephropathy (stones, benign prostatic hyperplasia, stictures, tumours).

The prevalence of chronic renal failure cases is increasing in Malaysia. According to the Malaysian Dialysis and Transplant Registry 2010, there were 4521 new dialysis patients in 2010 compared to 2112 new dialysis patients in 2001. The commonest primary renal disease of new dialysis patients was diabetic nephropathy (56%), followed by unknown cause (30%), hypertension (8%), glomerulonephritis (3%), systemic lupus erythematosus (1%), polycystic kidney (1%), and obstructive nephropathy (1%) (Lim *et al*., 2011).

Hemodialysis is a kind of renal replacement therapy for end stage renal disease. The early concept was first presented in 1854 by Thomas Graham of Glasgow about the principles of solute transport across a semipermeable membrane (Graham, 1854). Later, the artificial kidney was first developed by Abel, Rountree and Turner in 1913. They performed dialysis on animals (Abel *et al*., 1913). Georg Hass was the inventor of dialysis in humans. He performed the first time an extracorporeal dialysis successfully in humans in 1924. Kolff developed the clinically useful artificial kidney apparatus in 1943 (Kolff & Berk, 1944, Gordon *et al*., 2000).

The mechanism of hemodialysis applied the principle of diffusion across semi permeable membrane. The solutes will diffuse across the semipermeable membranes, followed the concentration gradient from high concentration to the low concentration.. Therefore, solutes like urea with higher concentration in the blood will diffuse across the membrane in the dialyzer to the dialysate fluid and bicarbonate with higher concentration in dialysate will diffuse to the blood. This principle allows removal of uraemic toxins and provides adequate balance of fluids, electrolytes and acid-base in hemodialysis (Figure 1.1).

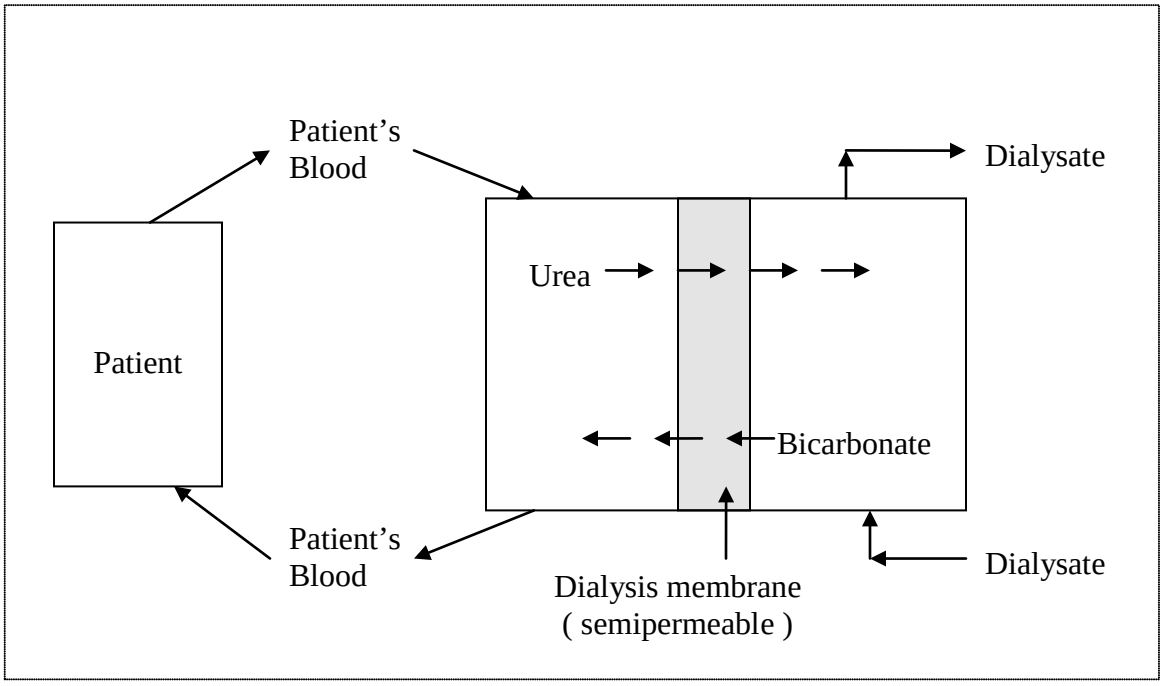

Figure 1.1: Schematic diagram of mechanism of diffusion in hemodialysis

There are systemic and ocular complication of hemodialysis either in immediate or long term effects of hemodialysis. The common systemic effects are low blood pressure, fatique, nausea and headaches because of removal of too much fluids or too rapidly. Serious systemic complications were reported such as thromboembolism, anaphylactic reaction, first use syndrome, bacteraemia, endocarditis, and stroke (LeSar et al., 1999, Liangos, 2005, Willicombe, 2010, Fitzgibbons, 2011, Wells & Foroozan, 2004).

Ocular abnormalities occur frequently in chronic renal failure patients on hemodialysis. These ocular manifestations are a result of uremia and abnormal electrolyte and fluid homeostasis that occurs with hemodialysis. Ocular abnormalities such as low or raised intraocular pressure during hemodialysis, cataract , band keratopathy, calcification of cornea and conjunctiva, retinal detachment, macular leakage,retinal hemorrhage, anterior ischemic optic neuropathy and uremic optic neuropathy (Eastherbrook & Mortimer, 1970, Popa & Nicoara, 2000, Evans & Rosner, 2005).

Cataract is the long term effect of end stage renal failure and chronic hemodialysis (Berlyne *et al*., 1972, Koch et al., 1976, Stein & Godel, 1980, Kazi *et al*., 1984, Haviv *et al*., 1999, Evans & Rosner, 2005). High blood urea and hypocalcemia in end stage renal failure(ESRF) contribute to cataract formation. One theory was that urea trapping in the lens causes chronic water accumulation within the lens lead to an osmotic cataract (Berlyne *et al*., 1972). Bilateral cataract due to hypocalcemia secondary to renal failure were found in young patients (Berlyne *et al*., 1972, Koch et al.,1976, Stein & Godel,

1980, Kazi *et al*., 1984). In hemodialysis, there is intermittent fluxes of fluid into and out of lens which lead to cataract formation (Evans & Rosner, 2005). Chronic hemodialysis has been shown to contribute to the development of rapid progress of cataracts in patients with chronic renal failure (Haviv *et al*., 1999).

So far, there were studies on intraocular pressure changes during hemodialysis. Some reported raised intraocular pressure during hemodialysis (Sitprija *et al*., 1964, Gafter *et al*., 1985, Cecchin *et al*., 1986, Tawara *et al*., 1998, Tovbin *et al*., 2002) and some reported differently (Ramsell *et al*., 1971 , Gutmann and Vaziri, 1984, Rever *et al.,* 1981, De marchi *et al.,* 1989). In low intraocular pressure, it is due to ultrafiltration process. Ultrafiltration during hemodialysis lead to gradual reduction of extracellular fluid compartment. This increase the oncotic pressure of extracellular space. Subsequently, draw fluids out from the surrounding tissues and decrease aqueous humour production lead to low intraocular pressure (Tokuyama *et al*., 1998). In raised intraocular pressure, it is due to rapid removal of uremic toxins. Rapid removal of uremic toxins and other solutes from the vascular compartment during hemodialysis lead to decrease serum osmolality. These serum osmolality is lower more rapidly than ocular osmolality lead to water movement into the aqueous humor. Subsequently, increased aqueous humor production and raised intraocular pressure (Watson & Greenwood, 1966, Tawara *et al.*, 1998). Significant raised intraocular pressure occurs especially in patients with existing impaired aqueous outflow such as narrow or closed angle (Tawara *et al.,* 1998, Yoon *et al.*, 2000, De Marchi *et al*., 1989).

Significant elevation of IOP is an important risk of glaucoma that causes irreversible ganglion cell damage. Excessive elevation of intraocular pressure leading symptomatic eye pain, headache and blurring of vision during hemodialysis (Cechhin *et al.,* 1986, Tawara *et al.,* 1998, Minguela *et al*., 2000, Yoon *et al*., 2000). Miguela *et al*. (2000) reported that there were symptomatic ocular pain in diabetic patient during hemodialysis. By alteration the dialysis parameter and added a colloid solution at the beginning of hemodialysis, the elevation of intraocular pressure was prevented and the patient became asymptomatic. However, other studies showed that changes of IOP was not statistically significant (Broekema *et al*., 1988, Hojs & Pahor, 1997). Broekema *et al*. (1998) conducted a study of intraocular pressure changes during hemodialysis, they found that there were no significant intraocular pressure changes at hourly interval for 4hours of hemodialysis in 14patients. Hojs & Pahor (1997) found that there were no statistically significant differences of intraocular pressure before and after hemodialysis and also no correlation between intraocular pressure, blood pressure and body weight changes.

Changes of intraocular pressure during hemodialysis are influenced by the serum osmolality and the aqueous outflow facility based on previous studies. Thereotically, The aqueous outflow facility is affected by the angle and depth of the anterior chamber. Changes in lens thickness are important and play role in alteration of anterior chamber depth and monitoring the cataract progression (Jivrajka *et al,* 2008).

Lens thickness is the anteroposterior diameter of lens. In normal person, lens thickness is 3.5mm at birth and 5mm in adult (Khurana, 2002). The normal central anterior

chamber depth is 3mm (Snell & Lemp, 1998). The lens thickness changes with age (Zadnik *et al.,* 1995, Richdale et al., 2008). Zadnik *et al.* (1995) reported the crystallines lens has been shown to thin nearly 0.20mm over 4 years from ages 6 to 10 years to compensate for an average increase in axial length of 1mm where as Richdale *et al.* (2008) found that the overall lens thickness increases linearly by 0.013 to 0.029mm/year because the crystalline lens continues to mature and more lens fibers are added within the capsular bag. The increased of lens thickness due to increased of the lens cell number and mass may account for the risk of development of cataracts (Shui & Beebe, 2008).

Praveen *et al*. (2008) found that lens thickness varied with axial length and age. Advancement in axial length associated with lens thickness decreased by 0.004mm. where as advancement with each decade of age, showed lens thickness increased by 0.155mm. Besides, there was significant decreased in anterior chamber depth by mean difference 0.44mm with advancement in lens thickness ($p<0.001$). In addition, Lim *et al*. (2006) revealed acute primary angle closure eyes had significant shallower anterior chamber depth and more anterior position of lens.

According to Schafer *et al*. (2006), they found recurrent elevation of intraocular pressure during hemodialysis. They reported raised intraocular pressure of 10-12mmHg and intumescence lens with ciliary block. Rapid decrease of serum osmolarity during hemodialysis lead to fluids flux in and out of lens and subsequently, lens swelling with ciliary block.

Dynamic equilibrium between the aqueous humour formation, outflow facility and episcleral venous pressure are essential to maintain the normal intraocular pressure. Alteration of lens thickness leading to lens position and anterior chamber depth changes. The aqueous outflow facility is affected by the changes of the lens position and anterior chamber depth. The raised intraocular pressure becomes more significant during hemodialysis if the individuals have compromised outflow facility.

The outflow facility plays role in IOP changes during hemodialysis was reported by Tawara *et al*. (1998) and Yoon *et al*. (2000). Tawara *et al*. (1998) found that patients with impaired aqueous outflow had significant rise in intraocular pressure during hemodialysis. Yoon *et al*. (2000) reported that the intraocular pressure was elevated more than 4mmHg during hemodialysis in 20 of 36 post vitrectomy eyes (55.6%) compared to 18 of 138 non operated eyes (13%). Symptomatic high intraocular pressure was 5 of 36 post vitrectomy eyes (14%).The early post vitrectomy eyes have acute post operative compromised aqueous outflow. Therefore, increased the risk of elevation of intraocular pressure. IOP elevation was well compensated in the patients with normal aqueous outflow system (Tawara *et al*., 1998, Yoon *et al*., 2000). Therefore, individuals who have compromised aqueous outflow facility such as peripheral anterior synechiae, narrow or closed angle, tendency to have significant raised intraocular pressure and glaucoma attack during hemodialysis.

Aqueous drainage is influenced by age and disease. There are two normal anatomical areas of resistance to the circulation of aqueous humor in the eyes such as the area that

the anterior surface of the lens is in contact with the iris (iris lens resistance area) and the angle of anterior chamber where the aqueous leaves the anterior chamber to enter the veins. Diabetes mellitus and age are factors may increase the iris lens resistance . With increased with age, there are changes with trabecular meshwork such as thickening of the columns and deposition of melanin debris blocking the passages leading to decreased of aqueous outflow. Therefore, diabetic and old age individuals are tendency to have high intraocular pressure than others (Snell & Lemp, 1998).

1.2 A-SCAN AND PERKINS TONOMETER

A-Scan and Perkins tonometer are handheld instruments that suitable and convenient to measure lens thickness, anterior chamber depth and intraocular pressure of the eyes during hemodialysis. However, these instruments are operator dependent. Therefore, error of measurement is minimized by taking the average reading of multiple measurements by the same operator.

A-scan is the gold standard for both clinical and research to measure the thickness of crystalline lens and the depth of the central anterior chamber. A-scan works on the principle of ultrasound that the velocity of sound waves vary as they travel through different medium. Ultrasound is the sound waves that the sound frequency of greater than 20,000 Hz (20 KHz). In ophthalmology, A-scan ultrasound probes use a frequency of approximately 10 million Hz (10 MHz). This extremely high frequency allows excellent resolution of small structures. The velocity of sound is determined by the density of the

medium. Sound waves travel faster through solids than through liquids medium. The ultrasound passes through the eye and is reflected from the posterior corneal surface, the anterior and posterior surface of the lens, the retina and the sclera. The pulse-echo times are recorded. By determining the time for sound waves to travel through the crystalline lens and anterior chamber depth, the lens thickness and anterior chamber depth can be calculated. The faster the sound wave travels, the thinner the lens thickness and the shorter the anterior chamber depth.

There are other modalities of instruments that measure anterior chamber depth and lens thickness. Although the measurements and principles of the instruments are different. A-scan is still the gold standard measurements and the measurements are acceptable clinically. Hashemi *et al*. (2005) conducted a study for comparison of measurement of anterior chamber depth using A-scan ultrasonography (Echoscan), Orbscan II, and IOLMaster. They found that A-scan has the mean differences of anterior chamber depth compared to other instruments were very small and clinically negligible. The mean difference of anterior chamber depth between Orbscan II and Echoscan was -0.03 ± 0.12 mm and between IOLMaster and A-scan measurements was +0.09 ± 0.14 mm. Orbscan II measurements were lower than Echoscan measurements of anterior chamber depth where as IOLMaster showed higher than Echoscan measurements.

Zeng *et al.*(2008) found that the lens thickness measurements by anterior segment optical coherence tomography and A-scan ultrasonography were slightly different. Anterior segment optical coherence tomography measurements were significantly greater

than A-scan measurements by 0.135 mm in elderly and 0.101 mm in younger subjects. Among all of these instruments, A-scan is still the most convenient handheld instruments for lens thickness and anterior chamber depth measurements of the end stage renal failure patients during hemodialysis at hemodialysis unit.

The gold standard instrument to measure intraocular pressure is goldmann applanation tonometer. However, it is not a convenient instrument to measure intraocular pressure during hemodialysis because it needs to work together with a slit lamp. Perkins tonometer is a handheld tonometer that works with the same principle of goldmann applanation tonometer that based on Imbert-Fick principle. This principle states that the pressure inside the sphere (P) equals the force necessary to flatten its surface (F) divided by the area of flattening (A) , P =F/A. (Figure 1.2) (Kanski, 2003).

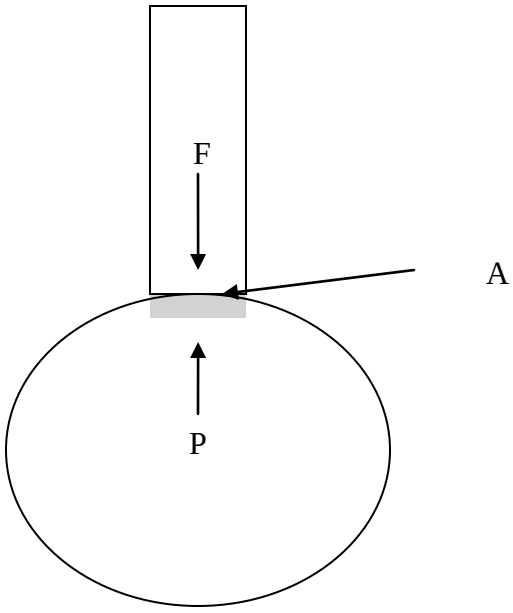

Figure 1.2: Imbert-Fick principle of applanation tonometry

The mean intraocular pressure measurements by perkins tonometer is slightly different than the goldmann applanation tonometer. Dos Santos *et al.* (1998) reported the mean difference between the goldmann applanation tonometer and perkins tonometer were 0.34 ± 0.69mmHg in the right eye and 0.33 ± 0.82mmHg in the left eye of the control group. In this study, they found goldmann applanation tonometry showed false elevated intraocular pressure readings in obese individuals due to transitory elevation of intraocular pressure. This elevated intraocular pressure was believed due to simultaneous breath-holding and thorax compression leading to increased venous pressure in obese individuals. The mean intraocular pressure was 20.9 ± 2.28mmHg in the right eye and 21.4 ± 3.16mmHg in the left eye of obese individuals by using goldmann applanation tonometer where as perkins tonometery showed 16.3 ± 2.39mmHg for the right eye and

16.3 ± 2.42mmHg for the left eye. Therefore, false diagnosis of glaucoma in obese individuals can be avoided by perkins tonometry.

The perkins tonometer was the most reliable in measuring intraocular pressure with significant less variability (Lim *et al.*, 2005). Lim *et al.* (2005) also found that tonopen XL, perkins tonometer and pneumatonometer underestimated the actual intraocular pressure. Perkins tonometer was more accurate than pneumatonometer where as tonopen has less inaccuracy than perkins tonometer.

1.3 RATIONALE OF THE STUDY

Elevation of intraocular pressure is a complication of hemodialysis. Lens thickness changes may result in alteration of anterior chamber depth that can compromise aqueous drainage. Individuals with compromised aqueous outflow facility have increased risk of symptomatic elevation of intraocular pressure during hemodialysis.

There were many studies on intraocular pressure changes during hemodialysis. but not on lens thickness and anterior chamber depth changes during hemodialysis. So far, no major or serial studies on the lens thickness changes during hemodialysis. Therefore, the significant of lens thickness changes during hemodialysis is still debatable. To the best of my knowledge, there is no data of lens thickness changes during hemodialysis in local study.

Evaluation of the lens thickness and anterior chamber depth with intraocular pressure changes during hemodialysis are essential. This will help us to determine whether the changes of lens thickness and anterior chamber depth with intraocular pressure are significant or not and to determine the important to have the baseline measurement of lens thickness prior to hemodialysis to anticipate acute intraocular pressure rise during hemodialysis in future. Based on these data of lens thickness changes during hemodialysis, it can help us to consider early removal of cataract and to prevent symptomatic elevation of intraocular pressure or acute angle closure glaucoma.

2.1 GENERAL OBJECTIVE

To determine the relationship of lens thickness and anterior chamber depth with intraocular pressure during hemodialysis.

2.2 SPECIFIC OBJECTIVES

(i) To determine the changes of mean of lens thickness during hemodialysis.

(ii) To determine the relationship of lens thickness(LT) and anterior chamber depth(ACD) during hemodialysis.

(iii) To determine the relationship of anterior chamber depth(ACD) and intraocular pressure (IOP) during hemodialysis.

(iv) To determine the relationship of lens thickness(LT) and intraocular pressure(IOP) during hemodialysis.

3.1 STUDY DESIGN

A cross sectional study was carried out to determine the relationship of lens thickness and anterior chamber depth with intraocular pressure during hemodialysis.

3.2 POPULATION, PLACE AND TIME

3.2.1 Study population

Subjects were recruited based on the selection criteria among the patients from Hemodialysis Unit, Queen Elizabeth Hospital.

3.2.2 Place of study

Hemodialysis Unit, Queen Elizabeth Hospital.

3.2.3 Period of study

November 2009 to December 2010

3.3 ETHICAL DISCLOSURE

The study was approved by Research and Ethical committee, Universiti Sains Malaysia and Health Ministry Malaysia. The study was conducted in accordance with the ethical standards stated in the Declaration of Helsinki of human research. Written and informed consent was obtained from all the subjects.

3.4 SAMPLING METHOD AND SAMPLE SIZE

3.4.1 Sampling Method

Simple random sampling

3.4.2 Selection of the Eyes

Each individual will be numbered and only one eye will be selected in the study. Right eye will be selected for those with odd number and left eye for even number. However, if the selected eye does not meet the criteria, the fellow eye will be selected in the study. Purpose of this randomization of eyes was to prevent selection bias.

3.4.3 Sample size

Sample size was calculated with power and sample size calculation software

PS Version 2.1.31

$\alpha = 0.05$

power =0.8

σ (Sandard deviation) = 0.56 (Jivrajka *et al*., 2008)

δ (Detectable difference) = 0.2

Estimated sample size-64

Estimated non responder- 10%

Sample Size required - 64 + 6= 70 eyes

3.5 SELECTION CRITERIA

3.5.1 Inclusion criteria

1) Patients on hemodialysis
2) Hemodialysis duration: 1month – 5years
3) Phakic eyes
4) Age between 20 to 70 years old

3.5.2 Exclusion criteria

1) Pseudopakic and aphakic eyes
2) Congenital ocular abnormalities
3) Cornea abnomalities

4) Ectopia lentis
5) Any known retinal or choroidal detachment
6) Any known glaucoma , uveitis or pseudoexfoliation
7) History of previous ocular trauma or surgery
8) High myopia and high hypermetropia

3.6 DEFINITION OF TERMS

3.6.1 Lens thickness

Crystalline lens in human is a transparent, biconvex structure situated behind the iris and the pupil and in front of the vitreous body. The center points on its anterior and posterior surfaces are anterior and posterior poles of the lens respectively. The line joining the poles forms the axis of the lens (Snell & Lemp, 1998). The lens thickness is the axis of the lens. It is also referred as the anteroposterior diameter of the lens. Lens thickness varies with age between 3.5mm at birth to 5mm in adult (Khurana, 2002).

3.6.2 Anterior chamber depth

Anterior chamber is the space that bounded anteriorly by the endothelial layer of cornea and posteriorly by the anterior surface of iris and part of ciliary body. Anterior chamber depth is divided to central and peripheral anterior chamber depth. At the peripheral part

of the anterior chamber depth is the corner between the cornea, sclera, ciliary body, and iris that referred as angle of anterior chamber. The central anterior chamber depth is 3mm in normal adults (Snell & Lemp, 1998). The anterior chamber depth has inverse association with age and spherical refractive errors (He *et al*., 2008). It is relatively shallow in very young children and old people (Khurana, 2002).

3.6.3 Intraocular pressure

Intraocular pressure refers to the pressure exerted by intraocular contents on the coats of the eyeball. Dynamic equilibrium between the aqueous humour formation, outflow facility and episcleral venous pressure are essential to maintain the normal intraocular pressure. The distribution of intraocular pressure within general population has a range of 11mmHg to 21mmHg. There is diurnal variation of intraocular pressure , with a tendency to be higher in the morning and lower in the afternoon and evening (Kanski, 2003).

3.6.4 Hemodialysis

Hemodialysis is a vascular access method of renal replacement therapy in renal failure based on the mechanism of diffusion of solutes across concentration gradient via a semipermeable membrane. It helps to remove waste products such creatinine and urea, as well as free water from the blood. It also provide adequate correction of fluid-electrolyte and acid-base abnormalities (Horl *et al*., 2004)

3.6.5 End stage renal failure

Kidney Diseases Outcomes Quality Initiative (K/DOQI) of the National Kidney Foundation (NKF) defines chronic kidney disease as either kidney damage or a decreased glomerular filtration rate (GFR) of less than 60mL/min/1.73m^2 for 3 or more months. End stage renal failure is the progressive loss of kidney function. The glomerular filtration rate (GFR) is less than 15 mL/min/1.73 m2 in end stage renal failure. Renal replacement therapy such as dialysis is needed at this stage (Eknoyan, 2002)

3.7 INSTRUMENTS

3.7.1 SCREENING INSTRUMENTS

(a) Snellen Acuity Chart

Snellen acuity chart (Rus IOL Enterprise, England) was used to assess the visual acuity of patients. The visual acuity of each eye was checked at 6 metres under normal room lighting.

(b) Slit Lamp Biomicroscope, Condensing lens and Tonometer

Nikon SL FS-3 (Nikon, Japan) slit lamp was used to examine the anterior and posterior segment of the eye. The posterior segment was examined with a 90D condensing lens (Volk, USA). The intraocular pressure was elicited with a goldmann applanation tonometer (Haag Streit, Switzerland).

(c) Retinoscope, Trial Lenses and Frame

Retinoscope (Heine, Germany), trial lenses and frame (Merck Sharp & Dohme, Italy) were used to assess the refraction status of the patients.

(d) Topical Eye Medication

Topical tropicamide 1.0% (Alcon, Spain) was used to dilate pupils for proper fundus examination. Topical proparacaine hydrochloride 0.5% (Alcon, Belgium) and fluorescein sodium/ Fluorets strip (Chauvin, England) were used to elicit the intraocular pressure.

(e) Goniolens and Coupling Gel

Goldmann 3-mirror lens (Ocular, USA) and hypromellose/ Genteal 0.3% (Norvartis, Switzerland) were used to assess the angle of the anterior chamber. The grading of angle

was based on Shaffer classification. Topical anaesthesia , proparacaine hydrochloride 0.5% (Alcon, Belgium) was applied to the eye prior to gonioscopy.

(f) Humphrey Visual Field Analyzer II

Assessment of visual field of patients was done with Humphrey visual field analyzer II (Carl Zeiss, Germany). The visual field was assessed in SITA Fast 24-2 with stimulus size 3 (1mm).

3.7.2 STUDY INSTRUMENTS

(a) A-scan

A-scan (Sonomed PAC SCAN 300 A, USA) was used to measure the lens thickness and anterior chamber depth of study subjects at 0hour, 2hour and 4hour of hemodialysis. A-scan was set in automatic mode with sound or tissue velocity (TVEL) 1532m/s for anterior chamber depth, 1641m/s for lens, and 1532m/s for vitreous. Topical anaesthesia was applied to the eye prior to A-scan examination (Figure 3.1)

(b) Perkins Tonometer

Perkins tonometer (Clement Clarke International, UK) is a portable, handheld applanation tonometer. It was used to measure the intraocular pressure of study subjects at 0hour, 2hour and 4hour of hemodialysis. Fluorescein sodium/ Fluorets strip (Chauvin, England) together with topical anaesthesia were applied to the eye prior to Perkins tonometer examination (Figure 3.1)

(c) Topical Anaesthesia

Topical proparacaine hydrochloride 0.5% (Alcon, Belgium) is a rapidly-acting topical anaesthetic that induced local anaesthesia lasting 10 minutes to 20 minutes.

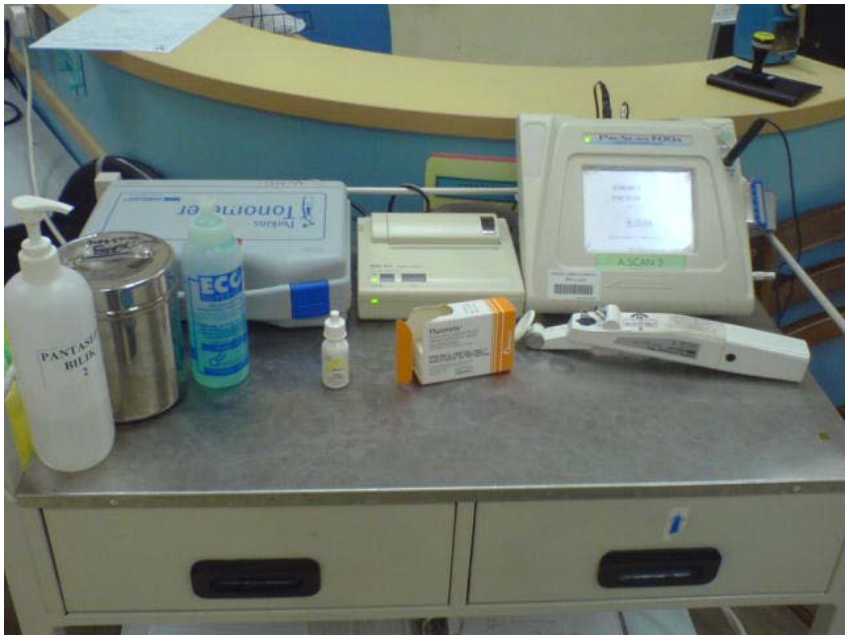

Figure 3.1: Mobile unit - A-scan and Perkins tonometer for lens thickness, anterior chamber depth and intraocular pressure measurement.