EFFECT OF ARGON LASER PAN RETINAL PHOTOCOAGULATION ON CORNEAL PARAMETERS AMONG PROLIFERATIVE DIABETIC RETINOPATHY PATIENTS

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ABSTRAK

Objektif

Aplikasi laser pada lapisan retina bermula dari permukaan kornea di mana permukaan kornea yang lutsinar akan memberi laluan kepada gelombang laser untuk sampai pada permukaan retina. Gelombang laser yang dilepaskan dari mesin laserakan memusnahkan saluran darah yang tidak normal pada lapisan retina dan merawat kawasan retina yang hipoksik. Pada masa yang sama, gelombang laser yang dilepaskan juga akan memberi kesan kepada lapisan kornea. Tujuan kajian ini dijalankan adalah untuk mengkaji tentang kesan laser Argon fotokoagulasi pan retina terhadap parameter kornea di kalangan pesakit proliferatif diabetik retinopati.

Metodologi:

Kajian ini merupakan kajian prospek kohort yang melibatkan pesakit yang baru di sahkan menghidap proliferatif diabetik retinopati yang menghadiri Klinik Oftalmologi Hospital Universiti Sains Malaysia, dari Jun 2017 sehingga Jun 2019. Struktur kornea yang diperiksa adalah ketebalan kornea pusat, ketumpatan sel endothelium dan koefisienvariasi sel endothelium. Imej kornea diperolehi dan di analisis menggunakan mikroskopspekular sebelum dan selepas laser Argon fotokoagulasi pan retina (minggu pertama dan minggu ke enam). Laser Argon fotokoagulasipan retina dijalankan dengan menggunakan mesin Zeiss Visulas 532.

Keputusan:

Seramai 33 orang pesakit terlibat dalam kajian ini. Dalam kajian ini, analisis statistik menunjukkan tiada perbezaan ketara pada min ketumpatan sel endothelium sebelum dan

selepas laser Argon fotokoagulasi pan retina (p= 0.876). Ketebalan kornea pusat dan koefisienvariasi sel endothelium sebelum dan selepas laser Argon fotokoagulasipan retina juga tidak menunjukkan perbezaan min yang ketara (p= 0.828 dan p= 0.074 mengikut turutan). Tiada sebarang korelasi diantara jumlah tenaga laser yang digunakan danparameter kornea dalam kajian ini (p> 0.05).

Kesimpulan:

Kajian ini mendapati laser Argon fotokoagulasi pan retinatidak memberikan kesan yang ketara kepada parameter kornea dikalangan pesakit proliferatif diabetik retinopati pada minggu pertama danminggu ke enam setelah selesai menjalani rawatan laser Argon fotokoagulasi pan retina. Kajian seterusnya masih diperlukan untuk memastikan keselamatan laser Argon fotokoagulasi pan retina kepada pesakit yang mempunyai masalah diabetik dan komorbid yang lain.

ABSTRACT

Objectives

Application of laser photocoagulation on the retina will start at a healthy and transparent central corneal surface so that laser waves cross the cornea to reach the retinal surface of area of interest to treat hypoxic and neovascularized area of the retina. The effect of laser photocoagulation to the cornea is mainly through thermal effect to the surrounding structures. The aim of this study was to document any effect of Argon laser pan retinal photocoagulation (PRP) on corneal parameters among proliferative diabetic retinopathy (PDR) patients.

Methodology:

This is a prospective cohort study involving newly diagnosed PDR patients who attended Ophthalmology Clinic Hospital Universiti Sains Malaysia from June 2017 till June 2019.The corneal structure was examined for central corneal thickness (CCT), endothelial cell density (CD) and coefficient of variation (CoV) of cell area. Images were obtained and analysed using specular microscope pre PRP and post completed PRP (at 1 week and 6 week post completed PRP). Laser PRP was performed using Zeiss Visulas 532 Nd Yag laser machine.

Results:

A total of 33 newly diagnosed PDR patients were included in this study. In this study, there was no significant reduction in the mean CD pre versus post argon laser PRP ($p= 0.876$). Neither CCT nor CoV showed statistical significant difference between pre and post completed PRP ($p= 0.828$ and $p= 0.074$ respectively). No correlation was found between amount of laser energy used and corneal cell parameters ($p>0.05$).

Conclusion:

In this study, we found that Argon laser PRP showed no significant effect on the corneal parameters (CCT, CD and CoV) among PDR patientsat 1 week and 6 weeks post completed PRP.Thus, further study of the issue is still required, as it remains to prove Argon laser PRP safety in patients with diabetic and other systemic co-morbididties.

1.1 BACKGROUND

Diabetes mellitus (DM) is an important public health concern. There is increasing in trend of the prevalence of diabetes globally. This is due to many factors such as population growth, aging, urbanization and increasing prevalence of obesity and physical inactivity. The prevalence of DM in Malaysia has escalated from 8.3% to 14.9% (1996-2006) and by 2030 it is predicted that 2.48 million Malaysians will be affected by DM [1]. Meanwhile, World Health Organization (WHO) Global Burden of Disease Study projected that the prevalence of DM is expected to increase to approximately 366 million by the year 2030 globally [2].

Diabetes is characterized by hyperglycemia and development of micro and macrovascular changes leading to morphological and functional changes in different organs. Ocular complications related to diabetes are varies from corneal abnormalities, glaucoma, iris neovascularization, cataracts, and neuropathies [3].

Duration of diabetes is a major risk factor associated with the development of diabetic retinopathy (DR). After 5 years, approximately 25% of Type 1 DM patients will have retinopathy. After 10 years, almost 60% have retinopathy, and after 15 years, 80% have retinopathy [4].

DR can be graded into categories of no apparent diabetic retinopathy (no DR), non-proliferative diabetic retinopathy (NPDR), proliferative diabetic retinopathy (PDR) and advance diabetic eye disease (ADED) [5].PDR and ADED are major causes of blindness among patients with DM and are associated with an increased risk of cardiovascular disease,

diabetic nephropathy and mortality [6]. PDR was found to be a prevalent complication among 23% of the younger-onset group, 10% in the older-onset group that takes insulin, and 3% in the group that does not take insulin [6].

In Malaysia, the 2007 Diabetic Eye Registry reported the prevalence of PDR was 7.1% [7]. Meanwhile, a recent study conducted in a primary care setting on Borneo Island in 2011 reported the prevalence of PDR was 3.2% [8]. Another study done among type 2 DM patient in Asian countries revealed that the prevalence of DR, PDR, and NPDR was 28%, 6%, and 27% respectively in T2DM. [9].

Pan retinal photocoagulation (PRP) is one of the treatments for PDR. It involves protein denaturation and is the result of tissue absorption of radiant energy with conversion to heat [10]. The Diabetic Retinopathy Study (DRS) showed that the risk of severe visual loss in patients with high risk characteristics is reduced by 50% at 2 and 5 years by PRP laser therapy and by up to 70% in moderate risk patients [11].Study also found that patients with PDR alone who received initial or early PRP has less chance of undergoing pars plana vitrectomy treatment within 2 years compared to those patient receiving PRP for PDR and vitreous haemorrhage or fibrosis [12].Other retinal conditions treatable with laser photocoagulation include diabetic macular oedema (DMO), retinal vein occlusions, leaking arterial macro aneurysms, age related macular degeneration (AMD), retinopathy of prematurity (ROP) and retinal tears. For each condition, laser is targeted at different tissue types in distinct areas of the retina [13].

Although PRP has been shown to be effective in retarding much of the morbidity associated with PDR, there are risks and complications associated with its use for example retinal and choroidal hemorrhages, pre-retinal membrane contraction, exudative detachments, and changes in the visual field. Apart from that, anterior segment complications such as iris atrophy, corneal oedema, epithelial erosions, and corneal neovascularization have also been documented. Bullous keratopathy and other corneal complications may be a result of endothelial cell destruction or decreased cell function due to photocoagulation [14].

DM itself has been found to have some negative effect on corneal endothelial parameters [15]. Corneal complication due to diabetes may be due to anatomical and physiological changes in every part of the cornea including epithelium, stromal as well as endothelium. A study reported that the mean central corneal thickness (CCT) was found to be thicker in diabetic patient compared to the non-diabetic population. While corneal endothelial density (CD) was lesser in diabetic group compared to normal population [16]. Meanwhile, Larsson L et al, also reported that abnormalities of corneal endothelial morphology such as polymorphism, polymegatheism, decrease in percentage of hexagonal cells, higher coefficient of variation (CoV), and increased CCT have been detected on specular microscopy in persons with diabetes [17].

McNamara NA et al, suggested that hyperglycaemic state alters endothelial structure leading to endothelial dysfunction and hydration of cornea and hence increased corneal thickness [18]. The mechanism on how diabetic or hyperglycaemic condition alters corneal endothelial CD was mainly due to sorbitol accumulation within cellsand a decrease in $Na^{+/}K^{+}$ ATPase activitywhich induce dysfunction of the corneal endothelium cell layer. Dysfunction of the

corneal endothelial cell will cause reduction in endothelial CD which will also lead to corneal hydration and caused increased in CCT measurements. Thus, corneal thickness indirectly informs about the function of the endothelial layer [19].

1.2 RATIONALE OF STUDY

Corneal endothelial was found subject to damage by surgical trauma and laser refractive surgery. There is still lack of study to evaluate the effect of PRP on corneal parameters among PDR patients. Thus, the aim of this study was to documentany alteration of corneal parameters CCT, CD and CoV after Argon laser PRP in PDR patients. By knowing the effect of Argon laser PRP on corneal parameters, we can improve the management of the patient in order to avoid the complication of the Argon laser PRP to the corneal endothelial cells.

1.3 LITERATURE REVIEW

1.3.1 DIABETES MELLITUS

DM is one of the most common chronic diseases in nearly all countries, and continues to increase in numbers and significance.It is a chronic disease that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces.Generally, DM can be classified as Type 1 DM and Type 2 DM.

Type 1 DM is characterized by deficient insulin production and requires daily administration of insulin. This type of diabetes is usually childhood onset.Type 2 DM resulted from the body's ineffective use of insulin. It comprises the majority of people with diabetes around the world, and is largely the result of excess body weight and physical inactivity. Both type of diabetes may cause severe end organ damage [20].

Diabetes complication can be divided into microvascular (due to damage to small blood vessels) and macrovascular (due to damage to larger blood vessel). Microvascular complications include damage to eyes (retinopathy) leading to blindness, to kidneys (nephropathy) leading to renal failure and to nerves (neuropathy) leading to impotence and diabetic foot disorders (which include severe infections leading to amputation). While macrovascular complications include cardiovascular diseases such as heart attacks, strokes and insufficiency in blood flow to legs [21].

Pertaining to the eye complication, patients with diabetes often develop ophthalmic complications, such as corneal abnormalities, glaucoma, iris neovascularization and cataracts. The most common and potentially most blinding of these complications, is DR [22].

1.3.2 DIABETIC RETINOPATHY

DR is one of the end organ damage complications of long standing or uncontrolled diabetic. It is an ischemic disease which are characterised by capillary non perfusion and a lack of blood flow and oxygen. Vascular endothelial growth factor (VEGF) will be stimulated following hypoxic insult, thus resulting in neovascularisation and oedema formation [13]. Other than duration and control of diabetic, pre-existing co-morbidities such as hypertension, chronic kidney disease, cerebrovascular accident, and hyperlipidemia are among the risk factors associated with development of DR [5]. Obesity, inactive lifestyle, smoking and pregnancy also related with the risk of DR formation**[**5**].**

The Early Treatment Diabetic Retinopathy Study (ETDRS) classify DR into NPDR and PDR. The classification of DR based on ETDRS is shown in Table 1.

Table 1: Classification of Diabetic Retinopathy based on ETDRS

Disease Severity	**Findings on dilated fundoscopy**
No retinopathy	No abnormalities
Mild NPDR	Presence of microaneurysm only
Moderate NPDR	More than just microaneurysm but less than severe NPDR
Severe NPDR	No sign of PDR with any of the following: - > 20 of intraretinal hemorrhages in each of 4 quadrant - Venous beading in ≥2 quadrant - Prominent intraretinal microvascular anomalies in ≥1 quadrant
PDR	Mild to moderate - New vessel on the disc (NVD) < 1/3 disc area - New vessel elsewhere (NVE) <1/2 disc area High risk - NVD >1/3 disc area - Any NVD with vitreous or pre retinal hemorrhage - NVE > ½ disc area with vitreous or pre retinal hemorrhage

A. Non Proliferative Diabetic Retinopathy (NPDR)

NPDR is characterised by varying degrees of microaneurysms, retinal haemorrhages, hard exudates, cotton wool spots, macular oedema, venous beading and loops, intraretinal microvascular abnormalities, and capillary non-perfusion.The 2007 report on 10,586 diabetics revealed that 63.3% of eyes examined had no DR. Meanwhile, 36.8% had any form of DR [23].Out of this, 50.7% has mild NPDR, 26.1% has moderate NPDR and 9.5% has severe NPDR[23].

Controlling diabetes and maintaining the glysocylated hemoglobin (HbA1c) level in the 6-7% ranges are the goals in the optimal management of diabetes and DR. If the levels are maintained, then the progression of DR is reduced [24]. Study by Pragaty G et al reported a significant association between severity of retinopathy and HbA1c values. They found that patients having good control of diabetic (HbA1C $\leq$ 7.0%) had low prevalence of retinopathy as compared to patients having moderate and poor control of diabetic (HbA1c values between 7.1-8.5% and HbA1c values >8.5%, respectively) [25].

Study also found that adequate scatter laser PRP reduces the risk of severe visual loss (< 5/200) by more than 50% [26]. Another study conducted by Liu and Xu, reported that the rate of improvement and unchanging visual acuity was 95.83% in NPDR group and 92.86% in pre PDR group after 3 to 6 month of laser photocoagulation [27].

DR screening schedule for patient with diabetic has been established in Malaysia by our Ministry of Health. This guideline aims for early detection of DR and its related

complications so that early referral and intervention can be done. According to the guideline, screening for DR should be done at time of diagnosis for adult with type 2 DM and at up to 3 years after diagnosis in adults type 1 DM. Screening for pregnant women with pre-existing DM and gestational DM (GDM) diagnosed in the first trimester should be done at the time of diagnosis[28]. For children with Type 1 DM, screening should be done at age 10 or at onset of puberty if this is earlier, after 2- 5 years of diabetes duration then annually thereafter [29]. While for children with type 2 DM, screening should be done at time of diagnosis [28].

B. Proliferative Diabetic Retinopathy (PDR)

New vessel formation is the hallmark of PDR and is usually found in conjunction with variable degrees of the features in NPDR [30]. PDR can be further divided into early PDR and high risk PDR. Early PDR is characterized by NVD < 1/3 disc area or NVE < ½ disc area. While high risk PDR is defined as NVD>1/3 disc area or any NVD with vitreous haemorrhage or pre retinal hemorrhage, or NVE > ½ disc area with vitreous or pre retinal haemorrhage [31].

It was estimated that 17 million of diabetic patients worldwide have PDR. [32]. While in Malaysia, it was found that the prevalence of PDR in Malaysia was 11.4 % [28]. A study reported that the prevalence of PDR was 6 fold higher in patients with early-onset than late-onset type 2 DM [33].

Vision loss occur in approximately 25% of patient with diabetic retinopathy is associated with proliferative disease. Without treatment, more than half of the patient with high risk PDR will be blind within 5 years [34].

Pan retinal photocoahulation has been established as an effective treatment to reduce by 50% the incidence of severe vision loss, if performed prior to the development of vitreous haemorrhage and tractional detachment. [35].Study conducted by Kaiser RS et al reported that there 76% of eyes with good visual acuity at baseline maintained good visual acuity at 1 year after PRP[36].

1.3.3 CORNEAL PARAMETERS

The cornea is the clear layer in front of the iris and pupil. It protects the iris and lens and helps focus light on the retina. It is composed of cells, protein, and fluid.The cornea is comprised of five layers: the epithelium, Bowman's layer, the stroma, Descemet's membrane, and the endothelium. Specular microscope is a tool to assess the corneal structures such as central corneal thickness (CCT), corneal endothelial cell density (CD) and corneal endothelial cell coefficient of variation (CoV).

A. Central Corneal Thickness

CCT is the thickess part of the cornea at its center. The mean value of the CCT in normal eyes is 554.78 (SD 32.61) µm. The peripherial corneal thickness is thicker than the central part. Among the peripheral corneal thickness, the thickest part is in the position of 12 o'clock, while the thinnest part is in the position of 6 o'clock [37].

CCT can be affected by various factors including intra-ocular pressure (IOP), longer axial length, and greater radius of corneal curvature, as well as higher body mass index (BMI), metabolic syndrome, and CKD [38]. CCT in diabetic patient was also found to be thicker compared to age and sex-matched healthy controls[39].

B. Corneal Endothelial Cell Density

Corneal endothelial cell is the innermost layer of the cornea. It consist of a single layer of hexagonal shape cell and it is non regenerating. The endothelium's main function is to control corneal hydration and nutrition with a leaky barrier formed by the apical gap and macula occludens junctions that keep some water out of the stroma but allow nutrients to pass, and with an ATPase-dependent metabolic pump that is located in the lateral plasma membranes. Endothelial wound healing involves flattening and enlargement of cells to maintain an intact monolayer as well as production of abnormal collagenous material posterior to Descemet's membrane [40].

At birth the CD ranges between 4000 cells/mm^2 and 5000 cells/mm^2. However, this value will decline with aging to approximately 2000 to 3000 cells/mm^2 in a normal adult eye. CD of 500 cells/mm^2 or less is one of the predisposing factors of corneal decompensation, which may eventually result in corneal oedema [41].

CD was found to decrease with age. A history of DM and ocular surgery were also associated with a lower CD[42].

C. Corneal Endothelial Cell Coefficient of Variation

The corneal endothelium consists of cells of varying surface areas. The polymegethism value is a coefficient describing the variation in cell area. As the standard deviation of the average cell area increases, the accuracy of the estimated true CD decreases. Therefore, increases in polymegethism causes a decrease in the accuracy of the average cell area. Polymegethism is defined by the CoV value determined with the equation below:

$$CoV = SD_{cell\ area} / mean\ cell\ area, \mu m^2$$

with CoV as coefficient of variation and SD as standard deviation of the mean cell area [43].

The CoV in the cell size among Malay was 58.1 (SD 22.6)% (range, 26.8 – 134) [44]. The average size of endothelial cells, standard deviation (SD) of cell size and CoV of cell area were found to be higher in diabetics [45]. Polymegathism is one of the early signs of endothelial disease which characterised by abnormal variation in the shape of endothelial cells and it also reflects an abnormal rate of endothelial wound repair [46].

1.3.4 DIABETES MELLITUS AND CORNEAL PARAMETERS

Patients with diabetes were found to have an abnormality of corneal endothelial morphology such as polymorphism, polymegatheism, decreases in percentage of hexagonal cells, higher CoV, and increased CCT on specular microscopy. Study found that persons with DM or higher HbA1c levels have greater CCT, independent of age, gender, or intraocular pressure (IOP) levels [47].The mechanism behind this was due to hyperglycemic condition that causes corneal endothelial dysfunction with resultant stromal hydration and swelling of the cornea [47].

A study done by Choo et al, found that Type 2 DM causes a significant alteration in the state of the cornea including reduction in endothelial CD and increased pleomorphism and polymegathism [45]. Endothelial CD in the diabetic group was significantly lower than that in the control group with value of 2541.6 (SD 516.4) and 2660.1 (SD 515.5) cells/mm^2 respectively [34]. Sorbitol accumulation within cellsand a decrease in $Na^{+/}K^{+}$ ATPase activitywill cause dysfunction of the corneal endothelium cell which eventually will lead to reduction in endothelial CD. These will also lead to corneal hydration and caused increased in CCT measurements. Thus, corneal thickness indirectly informs about the function of the corneal endothelial cell layer [19].

Minu R, et al,also found that there was a significant increase in CoV in diabetic group over controls. The CoV was 42.19% and 37.15% respectively [46].The changes in corneal endothelial cell CoV is also due to increased levels of aldose reductase activity in both the epithelium and endothelium. Corneal oedema may result from an abnormally high level of sorbitol in the endothelium, which interferes with the $Na^{+/}K^{+}$ ATPase pump [46].

Table 2 shows the distribution of normal corneal parameters based on previous studies.

Table 2: Normal Corneal Parameters Based On Previous Study

Corneal parameters	Normal value	Study
Central corneal thickness (CCT)	554.78 (SD 32.61) µm	Feizi S et al, 2014
Corneal endothelial cell density (CD)	2660.1 (SD 515.5) cells/mm^2	Choo MM et al, 2010
Coefficient of Variation (CoV)	58.1 (SD 22.6)%	Mohammad-Salih PA, 2011

1.3.5 LASER PAN RETINAL PHOTOCOAGULATION

There were various lasers thathad been used in the past. The Argon blue-green laser (70% blue 488 nm, 30% green 514.5 nm) was the predominant ophthalmic laser used for many years [48]. It was utilised for extrafoveal choroidal neovascular membranes in AMD, PRP in DR and to seal breaks in rhegmatogenous retinal detachment. However, it is now out of favour due to its short wavelenght which require high energy to produce adequate coagulation thus the potential for photochemical damage also higher for short wavelengths laser [49]. Currently, the green wavelength laser is superior due to minimal absorption of xanthophyll coupled with strong affinity for melanin and haemoglobin. Therefore, it can be used in the macular region as well as the periphery, and can target abnormal vessels. Green laser is available in two systems: argon gas (514.5nm) and solid state frequency doubled Nd-YAG (532nm) [13].

Argon laser obtains its energy delivery in the ions of Argon gas. It has an ability to produce tens of watts of continuous wave power in the region of blue (488 nm) and green (514.5 nm) wavelengths. Selected tissues, such as retinal pigment epithelium (RPE), can be heated by thermal reaction, classified as photocoagulation, and induced by the Argon laser. Because melanin in RPE cells absorbs wavelengths in the range of Argon better than those in the range of other ions of noble gas, it is the preference for photocoagulation of the RPE. In addition, since the blue wavelength of Argon can cause damage to inner retina, the green wavelength is more commonly used for photocoagulation of the neurosensory retina and RPE [50, 51].Argon green laser photocoagulation has been the most common standard treatment for diabetic maculopathy with DME and continues to be a treatment option even in the era of intravitreal pharmacotherapy. The effects of therapy are controlled by exposure time, power, spot size [48].

The Nd: YAG laser is a solid state laser that uses a neodymium-doped yttrium aluminium garnet (YAG) crystal as the laser medium. It is optically pump with a lamp or diode and most commonly emit light at 1064 nm. It can be used in either a pulsed or continuous mode. Pulse YAG lase are typically Q-switched to achieve high intensity pulse which can be frequency doubled to emit light at 532 nm. Solid state frequency doubled Nd-YAG (532nm) is also highly absorbed by haemoglobin and melanin in retinal pigment epithelium and trabecular meshwork. It is commonly used nowadays in treatment of many retinal conditions (PDR, diabetic macular edema, vein occlusions etc.). It has many advantages when compared with conventional single spot laser, as it is produced at a very short duration (10-20 msec) compared to (100-200 msec) of conventional single spot one which leads to less collateral retinal damage. Other advantages include relatively stable scar size, less destructive same efficiency [52].

Photocoagulation effect produced by Argon and neodymium-YAG burns revealed morphologically similar lesionswith damage predominantly at the level of the retinal pigment epithelium and outer retina. The high repetition rate, pulsed frequency-doubled neodymium-YAG laser produced thermal tissue effects similar to the continuous wave Argon laser [52].

1.3.6 DIABETIC RETINOPATHY AND ARGON LASER PRP

The landmark Diabetic Retinopathy Study (DRS) found that PRP reduced the risk of severe vision loss in patients with PDR or severe NPDR by at least 50% compared with untreated eyes. PRP involves up to 2000 laser burns applied to the peripheral retina. PRP causes regression of neovascularisation and is currently the mainstay of treatment for PDR [53].

For DR treatment using laser PRP, the recommendations in the Early Treatment of Diabetic Retinopathy Study (ETDRS) for an initial treatment consisted of 1,200 to 1,600 burns of moderate intensity, 200-500-μm size, one-half to one-spot diameter spacing at 0.1-second duration, divided over at least two sessions.These guidelines are helpful as a frame of reference, but reasonable modifications may be applied to different clinical scenarios and do not necessarily represent an absolute start or endpoint of therapy. Regardless of the laser type or power, the goal is to achieve an adequate blanching with medium grey spots avoiding direct treatment of major blood vessels and retina within the temporal arcade. Regression of new vessels is characterised by blunting of the NV growing tips, or replacement with fibrosis [54].

Although PRP is highly effective at reducing vision loss, it is also associated with well-documented side-effects, particularly with regards to peripheral visual function, dark adaptation, and night vision. Apart from that, some patient may experience discomfort or pain. For this reason, ophthalmologists or retina specialists may, in rare cases, resort to retrobulbar or subtenon anesthesia. Shortening the laser pulse duration, specifically avoiding the long posterior ciliary nerves at the three and nine o'clock positions and breaking up the treatment into multiple sessions may improve the patient's experience. Choroidal effusions or choroidal detachment are other potential adverse effects of PRP. Although choroidal effusions are common following PRP, they generally resolve without treatment and seldom cause visual sequelae [55].

Complication from PRP may be reduced by using shorter pulse duration as there is less thermal spread. Thus, PRP treatment is less painful and creates a lighter, smaller burn with less collateral damage to the outer retina [56]. With shorter pulse duration there will be stability of burn size over time and evidence of healing with less scarring though more burns may be needed for equivalent therapeutic effect [57].

Anterior segment complications that had been reported are iritis, focal iris atrophy, inequality of pupil size, posterior synechiae, anterior subcapsular and cortical lens opacities and corneal leukomata may occur. Fortunately, majority of these complications may be prevented by adequate dilatation of the pupil, patient cooperation, and selective use of retrobulbar anesthesia [58].

1.3.7 ARGON LASER PRP AND CORNEA

A corneal abnormality that may result from PRP includes striate keratopathy, corneal oedema and epithelial erosion. These complications can occur in mild form and may also progress to severe complication such as persistent corneal oedema and bullous keratopathy [59, 60].

There are few mechanisms on how corneal endothelial cell can be damage during Argon laser treatment. Among the proposed mechanisms are direct focal injury, thermal damage, mechanical shock waves, iris pigment dispersion, transient rise in intraocular pressure, inflammation, turbulent aqueous flow, time-dependent shear stress on endothelium, chronic breakdown of blood–aqueous barrier and damage from bubbles that settled onto the endothelium [61].

The effect of laser photocoagulation to corneal endothelium is mainly through thermal effect to surrounding structure. It caused temperature rise of 20°C to 30°C above baseline body temperature and collateral temperatures rise up to 10°C to 20°C above the baseline [62].

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