A RANDOMISED CONTROLLED TRIAL ON EFFECTS OF CONTACT AND NON-CONTACT LASER PHOTOCOAGULATION THERAPY ON OCULAR SURFACE IN PATIENTS WITH PROLIFERATIVE DIABETIC RETINOPATHY

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DISCLAIMER

I hereby certify that the work in this dissertation is my own except for quotations, questionnaires and summaries which have been duly acknowledged.

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ABSTRAK

Abstrak

Penyakit permukaan okular kerap dijumpai pada pesakit diabetes melitus. Ia akan menjadi lebih teruk akibat dari rawatan laser sama ada secara kontak atau tanpa kontak sekiranya pesakit diabetes dikomplikasikan dengan proliferatif diabetik retinopati.

Objektif

Matlamat kajian ini adalah untuk mengkaji kesan laser secara kontak dan tanpa kontak terhadap perubahan permukaan ocular dan skor Indeks Penyakit Permukaan Okular (OSDI) pada pesakit proliferatif diabetik retinopati.

Kaedah Kajian

Kajian ini merupakan kajian terkawal secara rawak yang dijalankan di Hospital Universiti Sains Malaysia bermula dari Jun 2013 hingga Mei 2015. Pesakit yang menghidapi proliferatif diabetik retinopati telah dipilih dan dibahagikan secara rawak kepada 2 kumpulan (kumpulan laser kontak dan kumpulan laser tanpa kontak) dengan menggunakan kaedah pensampelan rawak sampul surat. Perubahan permukaan okular dinilai melalui ujian Schirmer, masa pemecahan filem air mata (TBUT) dan skor OSDI sebelum dan 3 bulan selepas rawatan laser. Analisis data dilaksanakan dengan menggunakan SPSS versi 22.0.

Keputusan

Seramai 60 mata daripada 34 pesakit (kumpulan laser kontak: 30 mata daripada 17 pesakit dan kumpulan laser tanpa kontak: 30 mata daripada 17 pesakit) telah dipilih

untuk kajian ini. Didapati tiada perbezaan signifikan dalam perubahan purata ujian Schirmer (p=0.378) selepas 3 bulan rawatan laser antara kedua-dua kumpulan. Walaupun terdapat peningkatan signifikan ujian TBUT selepas 3 bulan rawatan laser bagi kumpulan laser kontak (p=0.038), tetapi tiada perbezaan signifikan dalam perubahan purata ujian TBUT di antara kedua-dua kumpulan (p=0.549). Didapati perubahan purata skor OSDI menunjukkan peningkatan yang signifikan pada 3 bulan selepas rawatan laser bagi kumpulan laser kontak berbanding dengan kumpulan laser tanpa kontak (p=0.044).

Kesimpulan

Rawatan laser secara kontak menyebabkan perbezaan semakin teruk yang signifikan untuk ujian TBUT dan peningkatan skor OSDI. Namun begitu, laser tanpa kontak tidak semestinya mengurangkan kesan ke atas permukaan okular pada pesakit diabetik retinopati. Langkah penjagaan yang sewajarnya perlu diambil untuk menjaga permukaan okular untuk pesakit diabetik retinopati semasa rawatan laser.

ABSTRACT

Introduction

Ocular surface changes are commonly seen in diabetes mellitus. It can be made worse by either contact or non-contact laser photocoagulation (LP) in proliferative diabetic retinopathy (PDR).

Objective

The aim of the study is to evaluate the effects of contact and non-contact LP therapy on ocular surface changes and Ocular Surface Disease Index (OSDI) score in patients with PDR.

Methods

This is a randomized controlled trial in Hospital Universiti Sains Malaysia from June 2013 to May 2015. Patient with PDR was selected and randomized into 2 groups by using random sampling envelope method, Contact LP group and Non-contact LP group. Patients were evaluated for Schirmer test, tear film break-up time (TBUT) and assessment of OSDI questionnaire before treatment and 3 months post laser treatment. Statistical analyses were performed using SPSS version 22.0.

Results

A total of 60 eyes from 34 patients were recruited (Contact LP: 30 eyes from 17 patients and Non-contact LP: 30 eyes from 17 patients). There was no significant difference in mean change of the Schirmer test ($p=0.378$) at 3 months post treatment between the two groups. Although there was significant reduction in TBUT at 3 months post laser in

Contact LP group (p=0.038), but there was no significant difference in mean change of TBUT between the two groups (p=0.549). There was significant increased in mean change of OSDI score at 3 months post treatment in Contact LP group as compared to Non-contact LP group (p=0.044).

Conclusion

Contact LP resulted in significant worsening of TBUT and increasing in OSDI sore. However, non-contact LP may not minimize the effect of laser on ocular surface of diabetic retinopathy patients. Appropriate care should be given to the ocular surface of diabetic retinopathy patients during LP procedure.

CHAPTER 1

INTRODUCTION

Diabetic retinopathy is a progressive dysfunction of the retinal vasculature caused by chronic hyperglycemia. As the prevalence of type 2 diabetes mellitus rises, so do its attendant, microvascular complications.

Based on the Malaysia First Annual Report of the National Eye Database in 2007, the level of severity of diabetic retinopathy among eyes examined showed that 23.1% had mild to moderate non-proliferative diabetic retinopathy (NPDR), 3.0% had severe NPDR, and 6.2% had proliferative diabetic retinopathy (PDR), of which 2.0% was at advanced diabetic eye disease state (Goh *et al.*, 2007). Diabetic retinopathy is a chronic and potentially sight-threatening disease. It is the major cause of blindness in persons less than 30 to 69 years of age in developed countries (Watkins, 2003).

Several studies (Moss *et al.*, 2000; Kaiserman *et al.*, 2004) have shown that dry eye syndrome is more common among diabetic patients. International Dry Eye Workshop (DEWS) recently agreed the latest definition of dry eye as a multifactorial disease of tears and ocular surface that results in symptoms of discomfort, visual disturbance and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface. One study has shown that the degree of keratoepitheliopathy was severe, and the corneal sensitivity, tear film break-up time and tear secretion were significantly reduced in the diabetic patients (Yoon *et al.*, 2004).

Laser photocoagulation (LP) has become a valuable modality to treat diabetic retinopathy. The Diabetic Retinopathy Study (DRS) found that its use in panretinal photocoagulation has been shown to be resulted in more regression of neovascularization in PDR. Nevertheless, LP therapy is not without complications. It is reported that a statistically significant change in endothelial cell density in the six-week follow-up post laser therapy (Pardos *et al.*, 1981). A study in evaluating the effect of coupling solutions used during LP on the ocular surface of patients with type 2 diabetes mellitus was done and they concluded that the use of viscous coupling solutions during applanation contact lens-aided laser procedures may be detrimental for the corneal epithelium in poorly controlled diabetic pateints (Dogru *et al.*, 2004).

LP is one of the risk factors for ocular surface disease in diabetic retinopathy (Ozdemir *et al.*, 2003). In contact LP, direct contact of the laser contact lens and coupling fluid onto the ocular surface can cause direct trauma to the cornea, and this is made worse by friction during manipulation of the laser contact lens. On the other hand, while delivering non-contact LP, the eye is kept opened by a speculum and this could expose the cornea and lead to excessive dryness of the ocular surface.

The aim of this study is to evaluate the effects of contact LP and non-contact LP towards ocular surface disease in PDR.

1.1 Background

1.1.1 Diabetes Mellitus

Diabetes mellitus is a metabolic disorder of multiple etiology characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both. Diabetes mellitus is diagnosed when the fasting blood sugar level (venous) is more than 6.1 mmol/L or when 2-hour post glucose load (venous) is more than 10.0 mmol/L.

The long term effects of diabetes mellitus include macrovascular complications such as cardiovascular, peripheral vascular and cerebrovascular disease, and microvascular complications include retinopathy which can potentially lead to blindness, nephropathy and neuropathy.

1.1.2 Diabetic Retinopathy

One of the microvascular complications of diabetes mellitus is diabetic retinopathy which gained great popularity among researchers. Diabetic retinopathy is a major cause of acquired blindness in adults. Extended period of exposure to hyperglycemia leading to vascular endothelial damage which subsequently causing retinal capillary changes. Diabetic retinopathy has been classified according to the guidelines set out by the Early Treatment Diabetic Retinopathy Study (ETDRS) and the Diabetic Retinopathy Study (DRS). Based on EDTRS, diabetic retinopathy is classified into mild, moderate and severe nonproliferative diabetic retinopathy (NPDR) and PDR (ETDRS, 1991).

1.1.3 Proliferative Diabetic Retinopathy

PDR is a microangiopathy leading to microvascular occlusion and leakage, subsequently retinal hypoxia which may cause neovascularization on retina and optic disc, and occasionally new vessels formation on the iris. PDR can be further subdivided into

i) Early PDR with definite neovascularization

ii) High risk PDR with any one of the following:

   a. 1/4 to 1/3 disc area of neovascularization of the optic disc (NVD) with vitreous hemorrhage

   b. 1/2 disc area or more of NVD with or without vitreous hemorrhage

   c. 1/2 disc area of neovascularization elsewhere (NVE) with vitreous hemorrhage

The gold standard treatment of PDR is panretinal laser photocoagulation.

1.1.4 Laser Photocoagulation

Laser is an acronym for light amplification by stimulated emission of radiation. Laser photocoagulation (LP) is the mainstay of treatment for PDR. Laser therapy in PDR takes the form of pan-retinal photocoagulation (PRP), in which perhaps 2000-3000 large burns are applied to retina outside the central thirty-degree zones. This tends to encourage a reduction in the caliber of new vessels. PRP is effective in producing a “quiescent” retina. There are two methods of LP delivery, which is the contact LP via slit lamp laser system, and non-contact LP via laser indirect ophthalmoscopy (LIO) system.

1.1.4.1 Contact Laser Photocoagulation

Contact LP denotes the conventional way of LP whereby laser via the slit-lamp biomicroscope and the delivery of Argon green laser is transcorneal. Laser is delivered to the retina using the Mainster Wide Field contact lens and Goldmann's three-mirror contact lens with the patient sits at a slit-lamp with laser fibreoptic cable.

Advantages of contact LP are during delivering of laser, the operator will have more precision and control, especially when treating around the vessels arcade and optic nerve. In addition, more stability can be achieved with the aid of laser contact lens in cases of wandering eye movements. Laser contact lens can also help in stabilization of the lids for those with excessive blepharospasm (Minarcik *et al.*, 2010).

1.1.4.2 Non-contact Laser Photocoagulation

The indirect ophthalmoscope with a condensing lens also may be used transcorneally to photocoagulate the posterior segment. LP is delivered to retina with the aid of a 20D or 30D condensing lens. There is no direct contact of the condensing lens with patient's eye hence no coupling fluid used. Patient's eye will be held open by wire speculum and intermittently the cornea must be moistened by applying artificial tears eyedrops.

Indirect non-contact LP treatment provides a better view of the whole fundus as compared to slit lamp contact laser system. This significantly reduces the time for panretinal photocoagulation (Mizuno, 1981). It can also be used to treat eyes with partial vitreous hemorrhage and suitable for patients with various medical and psychological conditions preventing adequate contact laser treatment (Gurelik *et al.*,

2004). In cases of small pupil, the operator can perform LP better with the aid of a 28D lens (Minarcik *et al.*, 2010).

Disadvantage of non-contact LP is the requirement of placement of eye speculum which keeps the eye opened, thus exposing to the risk of ocular surface dryness during the procedure.

1.1.5 Ocular Surface Disease and Diabetes Mellitus

Ocular surface is a biological continuum of three major regions, the cornea, limbus and conjunctiva. Ocular surface disease is a constellation of inflammatory disorder involving eyelid, eyelashes, lacrimal gland, tear film, conjunctiva and cornea.

The ocular surface disease in diabetes is characterized by a disorder of tear quantity and quality, squamous metaplasia, and goblet cell loss (Dogru *et al.*, 2000). Ozdemir *et al* studied on the risk factors for ocular surface disease in diabetic patients, and found that laser PRP, poor metabolic control and PDR are high risk factors for tear dysfunction and ocular surface disease (Ozdemir *et al.*, 2003).

The prevalence of ocular surface disease in diabetes mellitus is higher than normal populations (Saprafka *et al.*, 1990; Kaiserman *et al.*, 2005; Cousen *et al.*, 2006). Diabetes mellitus is commonly associated with dry eye disease (Manaviat *et al.*, 2008; Burda *et al.*, 2013). Every layer of the cornea was shown to have changes in diabetic eyes, starting from the epithelial cells which demonstrate punctate epitheliopathy, persistent epithelial defect and delayed healing (Schultz *et al.*, 1981; Chikama *et al.*,

2007), abnormally fragile epithelium (O'Leary *et al.*, 1981), thickened epithelial basement membrance (Azar *et al.*, 1992) and abnormal morphologic characteristics in corneal endothelial cells (Larsson *et al.*, 1996). Decreased corneal sensitivity is also commonly seen in diabetic cornea (Ruben, 1994; Saito *et al.*, 2003; Yoon *et al.*, 2004; Cousen *et al.*, 2007, Neira-Zalentein *et al.*, 2011). Diabetic patients often have decreased Schirmer test measurement and tear film instability as demonstrated by reduced TBUT (Goebbels, 2000; Dogru *et al.*, 2004; Cousen *et al.*, 2007; Rahman *et al.*, 2007; Burda *et al.*, 2012; Burda *et al.*, 2013).

1.1.6 Ocular Surface Disease Associated with Laser Photocoagulation

Panretinal LP is the treatment for PDR performed in the clinic setting. A total of 1500-2000 burns were applied in one or more treatment sessions under direct visualization of the retina (Klein *et al.*, 1997). Prompt treatment is advisable and effective in retarding much of the morbidity associated with PDR (DRS, 1981). However, it is associated with various risks and complications (Zweng *et al.*, 1974; Little, 1976). Effects of LP towards anterior segment such as severe degree of striate keratopathy with Descemet's membrane fold was well documented (Kanski, 1975). When laser power used is too high, it can cause damage to the cornea and lens (Peyman *et al.*, 1984). Breakdown of blood-aqueous barrier with significant increase in aqueous flare was also found after retinal laser treatment and it persisted to a lesser extent after 3 months (Larsson *et al.*, 2001).

A study found that the use of viscous coupling solutions during applanation contact-lens-aided laser procedures may be detrimental for the corneal epithelium in poorly

controlled non-insulin dependent diabetes mellitus patients with peripheral neuropathy and coexisting aqueous deficiency (Dogru *et al.*, 2004). They postulated that it might be the greater friction on the ocular surface caused by more viscous agents during rotational maneuvers of the applanation contact lenses inflicts more damage to the basement membrane in aqueous-deficient diabetic eyes.

During non-contact LP, there's no direct manupilation of the ocular surface. However, the eye is kept opened by a speculum throughout the procedure and this could expose the cornea and lead to excessive dryness of the ocular surface.

Traditionally, PDR has been managed with slit lamp laser system with the usage of contact lens. Many practitioners use slit lamp laser system when treating PDR. A survey showed that 91% of respondents used slit lamp contact laser system, as compared to only 9% used binocular indirect non-contact laser (Pollack, 2003). Both methods of LP are effective and results in stabilization of PDR (Gurelik *et al.*, 2004). However, LP can generate a further impairment in the ocular surface and corneal sensitivity (Ozdemir *et al.*, 2002; Dogru *et al.*, 2004; Neira-Zalentein *et al.*, 2011).

Patients with ocular surface disease often presented with a wide range of complains, ranging from redness of the eye, grittiness, foregin body sensation, photophobia to blurred vision (Sayin *et al.*, 2015).

1.1.7 Assessment of Ocular Surface Disease

Evaluation of ocular surface disease can be performed using Schirmer test, tear film break-up time (TBUT), cornea staining with fluorescein or Rose Bengal stain, tear osmolarity, symptom questionnaire and many more (Dogru *et al.*, 2004; Yoon *et al.*, 2004; Rahman *et al.*, 2007; Figueroa-Ortiz *et al.*, 2011).

In this study, Schirmer test, TBUT and Ocular Surface Disease Index (OSDI) questionnaire were employed to assess the ocular surface changes.

1.1.7.1 Schirmer Test

Schirmer test is a simple and noninvasive office procedure to evaluate the quantity of the tear film by using filter paper. It was first decribed by Schirmer in 1903 and subsequently many variants in the technique were introduced in regards to the type of paper, position of the filter paper, with or without anesthesia.

Schirmer test with topical anesthesia (proparacaine hydrochloride 0.5%) is performed with standardized strips of filter paper. The anesthetic is thought to eliminate the reflex tearing produced by irritation from the filter paper, and wetting of the filter paper thought to represent basal tear secretion.

Previous studies noted that the Schirmer test results were significantly lower in diabetic patients (Dogru *et al.*, 2000; Yoon *et al.*, 2004). It was found that Schirmer test values averaged 7.40 ± 0.38 mm in diabetic patients versus 13.53 ± 0.50 mm in the control subjects ($p<0.001$); Schirmer test results were also lower in patients with poorly

controlled diabetes compared with diabetes with good control ($p<0.001$) (Dogru *et al.*, 2000).

1.1.7.2 Tear Film Break-up Time (TBUT)

TBUT is commonly known as one of the most effective, simplest and noninvasive test for diagnosing dry eye disease. It has high reproducibility (95%) in dry eye patients (Lee *et al.*, 1988). TBUT is a simple test to measure the relative stability of the precorneal tear film. It is performed with moistened fluorescein strips being introduced to the conjunctival sac with minimal stimulation. The subjects will be instructed to blink several times. TBUT is measured from the time interval between a complete blink and the formation of the first dry spot in the precorneal tear film after instillation of the fluorescein (Savini *et al.*, 2008). Few studies noted that there was statistically significant reduced in TBUT in diabetic patients as compared to control subjects (Dogru *et al.*, 2000; Li *et al.*, 2004).

1.1.7.3 Ocular Surface Disease Index (OSDI)

Ocular surface disesase can be evaluated subjectively by questionnaires The Ocular Surface Disease Index (OSDI). This questionnaire is developed by the Outcomes Research Group at Allergan Inc (Irvine, Calif). It is a 12-item questionnaire designed to provide a rapid assessment of the symptoms of ocular irritation consistent with dry eye disease and their impact on vision-related functioning.

The OSDI is assessed on a scale of 0 to 100, with higher scores representing greater disability. The index demonstrates sensitivity and specificity in distinguishing between normal subjects and patients with dry eye disease.

$$\text{OSDI} = \frac{(\text{sum of scores}) \times 25}{\text{number of questions answered}}$$

OSDI demonstrates both high internal consistency and good to excellent test-retest reliability in between patients with dry eye disease and normal controls. Other than that, OSDI also demonstrates excellent validity, effectively discriminating between normal, mild to moderate, and severe dry eye disease (Schiffman *et al.*, 2000).

The OSDI is a valid and reliable instrument for assessing severity of dry eye disease and it shows good sensitivity and specificity in distinguishing between normal subjects and dry eye patients (Schiffman *et al.*, 2000). Patients can be classified into normal (OSDI score less than 12), mild (13-22), moderate (23-32) or severe dry eye disease (score 33 or more) (Schiffman *et al.*, 2000). The translated Malay version of OSDI questionnaire was used in this study. The translated version was validated and conducted for study to assess patient with dry eyes [(Fadzillah MT. The Effect of Omega 3 on Dry Eye Disease, of dissertation submitted as partial fulfillment for the degree of Master of Medicine (Ophthalmology), Universiti Sains Malaysia 2013)]. Reliability of total items and subcategory were good with Cronbach alpha value of more than 0.7 in the mentioned study.

1.2 Rationale of Study

Several clinical and experimental studies have reported structural, metabolic, and functional abnormalities in the cornea of diabetic patients (Azar *et al.*, 1992; Larsson *et al.*, 1996; Dogru *et al.*, 2001; Chikama *et al.*, 2007; Cousen *et al.*, 2007; Hasan, 2010; Fuerst *et al.*, 2014). Diabetic patient are at higher risk of developing ocular surface disease as well as diabetic keratopathy.

Epithelial fragility, microcystic edema, superficial punctate keratopathy, persistent epithelial defects, recurrent corneal erosions, decreased corneal sensitivity, neurotrophic corneal ulceration, dry eye, filamentary keratitis, and Descemet fold constitute the range of diabetic corneal complications.

Friction from manipulation of laser contact lens and coupling fluid used during contact LP on the ocular surface may be detrimental for the corneal epithelium in poorly controlled non-insulin dependent diabetes mellitus. In non-contact LP, the eye is kept opened by a speculum throughout the procedure and this could expose the cornea and lead to excessive dryness of the ocular surface. Both contact and non-contact LP procedure could worsen the pre-existing diseased cornea and lead to devastating sequelae such as infective keratitis. Thus, it is important for clinician to understand this and be more vigilant in order to prevent the complications.

The aim of this study is to evaluate the effects of contact LP and non-contact LP towards ocular surface disease in PDR.

CHAPTER 2

RESEARCH OBJECTIVES

2.1 General Objective

To evaluate the effects of contact and non-contact LP therapy on signs and symptoms of ocular surface in patients with PDR.

2.2 Specific Objectives

1) To compare the mean change (baseline and three months post treatment) in Schirmer measurement between contact LP and non-contact LP in patients with PDR.

2) To compare the mean change (baseline and three months post treatment) in TBUT between contact LP and non-contact LP in patients with PDR.

3) To compare the mean change (baseline and three months post treatment) in OSDI score between contact LP and non-contact LP in patients with PDR.

CHAPTER 3

MATERIALS AND METHODS

3.1 Study Design

Randomised controlled trial

3.2 Place of Study

Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan

3.3 Study Duration

June 2013 to May 2015

3.4 Study Population

All diabetic patients with PDR presented to Hospital Universiti Sains Malaysia.

3.5 Ethical Board Approval

This study was approved by the Research and Ethical Committee, School of Medical Sciences, Universiti Sains Malaysia on 29th May 2013 (Appendix A).

3.6 Financial Support

This study did not receive any financial grant or support from any party.

3.7 Sample Size

This is a pilot study. Sample size is 30 eyes in each group.

3.8 Sampling Method

Universal sampling was used in which all Type 2 Diabetic Mellitus patients diagnosed with PDR attending Eye Clinic, Hospital Universiti Sains Malaysia from June 2013 till May 2015 that fulfill the inclusion criteria and exclusion criteria were recruited into the study.

3.9 Randomization

New cases of PDR who fits the eligible criteria and consented for the study were randomized into two groups using random sampling envelope technique. A stack of opaque envelope were prepared with half of the envelopes containing a piece of paper with the word “CONTACT LP” and the remaining halves stated “NON-CONTACT LP”. These envelopes were shuffled and drawn for each patient. This was performed after the baseline parameters had been taken.

3.10 Selection Criteria

All patients were assigned into two groups, Contact LP group and Non-contact LP group.

3.10.1 Inclusion Criteria

- Newly diagnosed PDR.
- Age between 18 to 70 years old.

3.10.2 Exclusion Criteria

- Patients on regular eye drops medication (eg topical antiglaucoma drugs or tears supplement)
- PDR with neovascular glaucoma
- Poor media that obscuring view of delivering LP to the retina
    a) Corneal opacity
    b) Preretinal or vitreous hemorrhage obscuring view of retina
- Previous history of intraocular surgery or ocular trauma including chemical, thermal or radiation injury
- Contact lens wearer
- Previous history of LP

3.11 Definition of Terms

3.11.1 Proliferative Diabetic Retinopathy (PDR)

PDR is a more serious form of diabetic retinopathy which characterized by presence of neovascularization on or within one disc diameter of the disc and/ or neovascularization elsewhere in the fundus (ETDRS, 1985).

3.11.2 Contact Laser Photocoagulation

Laser is delivered to the retina using the Mainster Wide Field contact lens and Goldmann's three-mirror contact lens with the patient sits at a slit-lamp with laser fibreoptic cable (Dowler, 2003; Minarcik *et al.*, 2010). Laser machine Visulas 532s (Carl Zeiss) was used in this study.

3.11.3 Non-contact Laser Photocoagulation

The binocular indirect ophthalmoscope laser delivery system with a 20D, 28D or 30D condensing lens is used transcorneally to photocoagulate the posterior segment (Dowler, 2003; Minarcik *et al.*, 2010). There's no direct contact of coupling fluid or laser contact lens with the ocular surface during the LP procedure.

3.11.4 Schirmer test

Schirmer test with anesthesia is a test to measure basal tear production using Schirmer test paper. Readings are reported in millimeters of wetting for 5 minutes. A reading less than 5 mm is taken as the cut-off value for abnormal (Dogru *et al.*, 2001).

3.11.5 Tear Film Break-up Time (TBUT)

TBUT is defined as the interval between the last complete blink and the first appearance of a dry spot or disruption in the tear film. A TBUT of less than 10 seconds is considered abnormal (Rahman *et al.*, 2007).

3.11.6 Ocular Surface Disease Index (OSDI)

Ocular surface disease index (OSDI) is a scoring system based on questionnaire consisting of 12 questions with scoring from 4 to 0. Patient is asked regarding visual function, ocular symptoms and environmental triggers for the past 1 week.

Based on the conversion chart for OSDI scoring system, patient can be classified into normal, mild, moderate or severe dry eye disease. OSDI score less than 12 is considered normal, 13-22 for mild, 23-32 for moderate and scoring of 33 or more is considered as severe dry eye (Schiffman *et al.*, 2000).

3.12 Instrument

3.12.1 Carl Zeiss Visulas 532s Laser System (Carl Zeiss Meditec AG, Jena, Germany)

This slit lamp laser system (Figure 3.1) is a frequency doubled solid state laser with 532 nm argon-green laser wavelength. It provides various sizes of laser spot option ranging from 50 μm^2 to 1000 μm^2 without using contact lens.

Figure 3.1 Carl Zeiss Visulas 532s Laser System

3.12.2 Carl Zeiss Visulas LIO 532s/Trion Laser System (Carl Zeiss Meditec AG, Jena, Germany)

Non-contact LP is delivered via this LIO system with the laser console similar to contact LP. Binocular indirect ophthalmoscope is being used instead of slit lamp biomicroscopy system. LP is delivered to the retina with the aid of a 20D condensing lens (Figure 3.2).

Figure 3.2 Carl Zeiss Visulas LIO 532s/ Trion Laser System

3.12.3 Ocular Mainster Wide Field Laser Contact Lens (Ocular Instruments Inc., WA, USA)

Ocular Mainster wide field contact lens (Figure 3.3) was one of the contact lens used for LP. It is used with coupling fluid. It provides excellent retinal resolution with binocularity across the entire field of view. It offers 118° field of view. The contact diameter with ocular surface is 15.5 mm.

Figure 3.3 Ocular Mainster Wide Field Laser Contact Lens

3.12.4 Goldmann's Three Mirror Laser Contact Lens (Ocular Instruments Inc., WA, USA)

Goldmann's three mirror laser contact lens (Figure 3.4) with coupling fluid was used to deliver LP to the periphery retina. This contact lens has three mirrors angled at 59°, 67° and 73° and the center portion of the lens permitting view to the posterior pole. The contact diameter with ocular surface is 18 mm.

Figure 3.4 Goldmann's Three Mirror Laser Contact Lens

3.12.5 Slit Lamp Biomicroscope (Topcon Corp., Japan)

The slit lamp biomiocroscope was used to perform detail ocular examination (Figure 3.5). In this study, it is used to assess the TBUT and also to exclude any pre-existing ocular pathology.

3.12.6 Fluorescein Sodium Paper Strip (Bio Glo) (HUB Pharma., USA)

Fluorescein sodium paper strip (Figure 3.6) was used to stain the ocular surface for assessment of TBUT.

Figure 3.5 Slit Lamp Biomicroscope

Figure 3.6 Fluorescein Sodium Paper Strip

3.12.7 Schirmer Test Paper (OptiTech Eyecare, India)

Schirmer test paper is a diagnostic sterile filter paper with gauge printed on the strip (Figure 3.7). It is used to measure basal tear production with instillation of local anesthesia.

Figure 3.7 Schirmer Test Paper

3.13 Medication

3.13.1 Guttae Tropicamide 1% (Alcon Laboratories, USA)

Topical tropicamdie 1% (Figure 3.8) is used for dilation of pupil for fundus examination. It is an anticholinergic drug which acts by blocking acetylcholine thus resulting in relaxation of iris sphincter muscle. The iris radial muscle which is innervated by adrenergic pathway is therefore unopposed and hence producing pupil dilatation.