"AN OBSERVATIONAL STUDY TO ANALYSE THE ROLE OF VISUAL EVOKED POTENTIAL IN VISUAL PROGNOSIS BEFORE AND AFTER PANRETINAL PHOTOCOAGULATION FOR DIABETIC RETINOPATHY IN TYPE 2 DIABETIC MELLITUS"

M.S. DEGREE

BRANCH –III (OPHTHALMOLOGY)

MAY 2019

GOVT. RAJAJI HOSPITAL &

MADURAI MEDICAL COLLEGE

MADURAI

THE TAMILNADU

Dr. M.G.R MEDICAL UNIVERSITY, CHENNAI.

TAMILNADU

CERTIFICATE FROM THE DEAN

This is to certify that the dissertation entitled **"AN OBSERVATIONAL STUDY TO ANALYSE THE ROLE OF VISUAL EVOKED POTENTIAL IN VISUAL PROGNOSIS BEFORE AND AFTER PANRETINAL PHOTOCOAGULATION FOR DIABETIC RETINOPATHY IN TYPE 2 DIABETIC MELLITUS"** submitted by **Dr.J.DHEEBALAKSHMI,** to the Faculty of Ophthalmology, The Tamilnadu Dr.M.G.R. Medical University, Chennai in partial fulfilment of the requirement for the reward of M.S. Degree in Ophthalmology is a bonafide work carried out by him during the period 2016-2019.

Place: Madurai

Date:

Prof.Dr.D. MARUTHUPANDIAN
M.S., F.I.C.S., F.A.I.S., FAC
Dean,
Madurai Medical College &
Govt. Rajaji Hospital, Madurai.

CERTIFICATE FROM THE HEAD OF THE DEPARTMENT

This is to certify that this dissertation entitled **"AN OBSERVATIONAL STUDY TO ANALYSE THE ROLE OF VISUAL EVOKED POTENTIAL IN VISUAL PROGNOSIS BEFORE AND AFTER PANRETINAL PHOTOCOAGULATION FOR DIABETIC RETINOPATHY IN TYPE 2 DIABETIC MELLITUS"** is the bonafide original work of **Dr.J.DHEEBALAKSHMI,** in partial fulfillment of the requirement for M.S.,(Branch III) Ophthalmology examination of the Tamilnadu Dr.M.G.R. Medical university to be held in May 2019.

Prof. Dr. K. KAVITHA M.S, D.N.B.,
Head of the Department,
Department of Ophthalmology,
Madurai Medical College, Madurai.

ANTI- PLAGIARISM CERTIFICATE

This is to certify that this dissertation work titled **"AN OBSERVATIONAL STUDY TO ANALYSE THE ROLE OF VISUAL EVOKED POTENTIAL IN VISUAL PROGNOSIS BEFORE AND AFTER PANRETINAL PHOTOCOAGULATION FOR DIABETIC RETINOPATHY IN TYPE 2 DIABETIC MELLITUS"** of the candidate **Dr.J.DHEEBALAKSHMI** with **Registration Number 221613102** for the done for award of Master of Surgery Degree in the branch of Ophthalmology. I personally verified the urkund.com website for the purpose of plagiarism check. I found that the uploaded thesis file contained from introduction to conclusion pages and result shows **7%** of plagiarism in the dissertation.

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DECLARATION

I, **Dr.J.DHEEBALAKSHMI** hereby solemnly declare that, this dissertation titled **"AN OBSERVATIONAL STUDY TO ANALYSE THE ROLE OF VISUAL EVOKED POTENTIAL IN VISUAL PROGNOSIS BEFORE AND AFTER PANRETINAL PHOTOCOAGULATION FOR DIABETIC RETINOPATHY IN TYPE 2 DIABETIC MELLITUS"** was done by me.

I also declare that this bonafide work / a part of this work was not submitted by me / anyone else, for any award, for Degree / Diploma to any other University / Board either in India / abroad. This is submitted to The Tamilnadu Dr. M. G. R. Medical University, Chennai in partial fulfillment of the rules and regulations for the award of Master of Surgery degree Branch -III (Ophthalmology) to be held in May 2019.

Place: Madurai **(Dr.J.DHEEBALAKSHMI)**

Date:

ACKNOWLEDGEMENT

I express my sincere thanks and gratitude to **Prof. Dr. D. MARUTHUPANDIAN M.S., FICS., FAIS.,** The Dean, GRH and MMC Madurai for permitting me to conduct this study. I am extremely grateful to **Prof. Dr.K.KAVITHA M.S, D.N.B.,** HOD**,** Professor of Ophthalmology and Associate Professor of Ophthalmology, GRH, MMC, Madurai, for their constant source of support and encouragement for completing this study. I have great pleasure in thanking my beloved guide **Dr.N.PARVATHASUNDARI M.S, DO.,** Associate Professor and all my Assistant Professors of Ophthalmology department at Madurai Medical College, Madurai, for their constant source of cheer and encouragement throughout the study.

I express my deep sense of gratitude to The Professor and HOD of Neuromedicine, for their support to this study.

I thank the Secretary and Chairman of the Institution Ethical Committee, GRH Madurai.

I am indebted to all the patients, paramedical staffs for their sincere co-operation for the completion of this study.

I am grateful to my fellow post graduate colleagues for their valuable help throughout this study.

I am extremely thankful to my family members for their constant support.

Above all I thank the almighty for guiding me with his blessings throughout this work.

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PART I

INTRODUCTION

Diabetic mellitus is chronic disease that increases the risk of developing multiple medical complications. So, this patients requires screening, long term observation for diagnosis, treatment and prognosis.

Diabetes mellitus is the major systemic cause of blindness in western world. It contributes 4.8% of the 37 million cases of blindness throughout the world.

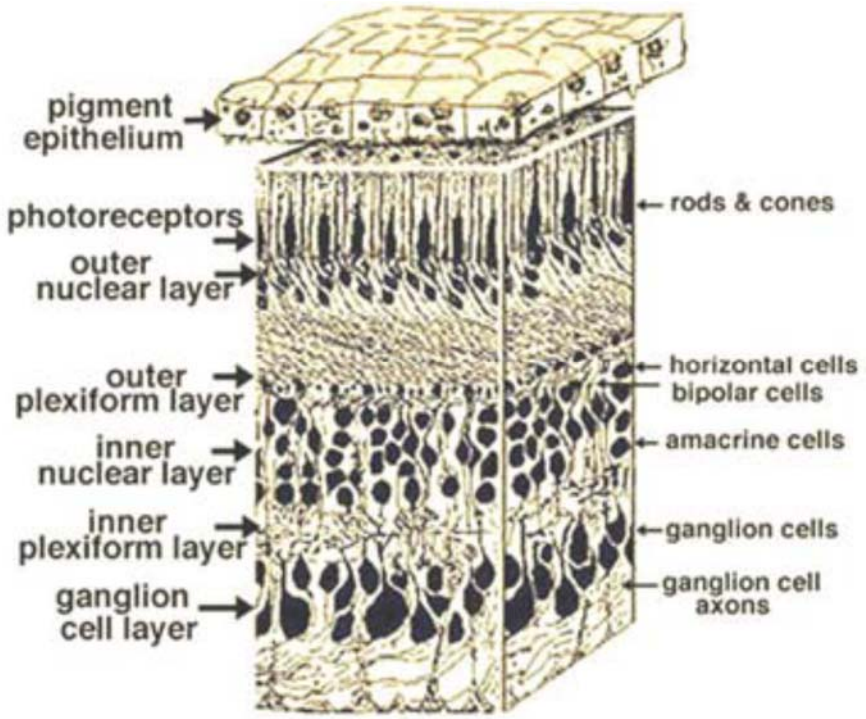
Impact of Diabetic over vision can be significantly reduced by proper glycemic control, routine ophthalmological examination and proper treatment.

Laser photocoagulation remains the mainstay of treatment for established diabetic retinopathy .it has been shown to reduce visual loss due to diabetic macular edema and proliferative Diabetic Retinopathy.

DIABETIC RETINOPATHY

Retina is a ten layered sheet and most metabolically active organ in the body which composed of neurons, photoreceptors and supporting cells. The outer one third of retina receives its blood supply from the choriocapillaris and the inner two third of the retina is supplied by central retinal artery, a branch of ophthalmic artery.

FIGURE 1 : RETINAL LAYER



TRANSPARENCY OF RETINA

Transparency of retina should be maintained so that light should pass through layers of retina and activate posteriorly situated photoreceptors.

- Retinal nerve fibres are unmyelinated since myelination can block light rays. As such, it requires more energy to more energy than myelinated axon for maintain membrane potential.
- Vasculature density is low at inner retina .so,it is at constant state of relatively hypoxia.

- Inner retina has only few mitochondria since it can block light transmission. so it depend on glycolysis for energy production rather than oxidative phoporylation.

So, retina remain most metabolically active even in the low oxygen tension.whenever oxygen demand is increased inner retina more prone for retinopathy.

BLOOD RETINAL BARRIER

In the human brain, there is selective exchange of molecules between blood vessel and neural parenchyma is regulated tightly by the structure called blood-brain barrier (BBB). As a extension of CNS, retina also has tight barrier called blood-retinal barrier (BRB).

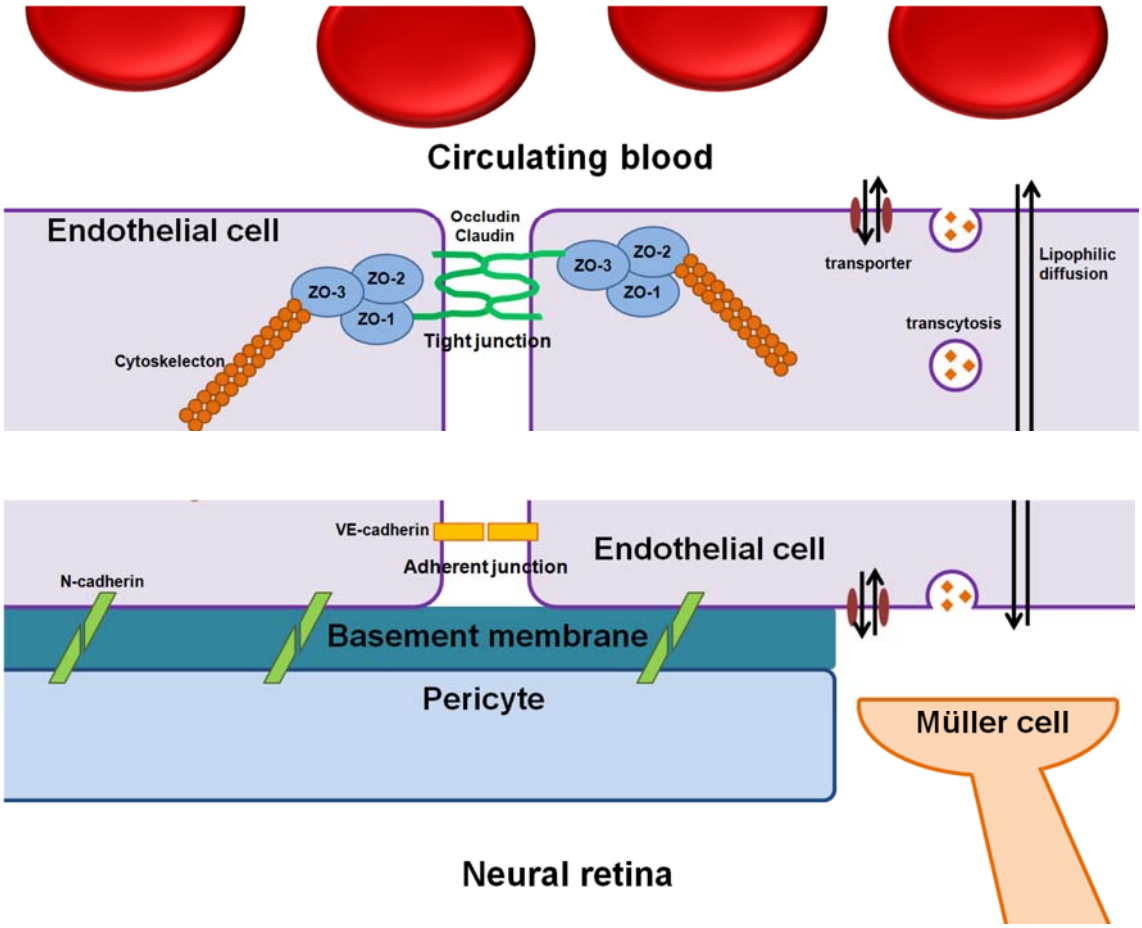
Neural retina receives dual blood supply from retinal vessels and choroidal vessels. Neural retina is separated from retinal vessels and choroidal vessels by inner and outer BRB, respectively.

- Inner BRB is formed by a tight junction between adjacent retinal vascular endothelium (resembles the BBB proper of brain)
- Outer BRB formed by a tight junction between adjacent retinal pigment epithelium (resembles the blood-CSF barrier of brain).
- Among these two kinds of BRB, abnormality in the inner BRB due hyperglycemia is responsible for the of diabetic retinopathy.

Inner blood-retinal barrier is consist of multiple cellular component including endothelial cells, pericytes and Müller cells. Pericytes ensheath the retinal microvascular endothelium and share their common basement membrane with retinal endothelial cells.

- Pericytes are adherant to endothelial cells by the N-cadherin mediated adherent junction. Müller cells have spatial proximity with endothelium cells and connect with endothelium by their footprocesses. Each adjacent endothelial cells are interconnected with each other through their tight junctions and act as a functional barrier.
- Selective permeablity of molecules through the paracellular pathway is tightly regulated by this tight junction and controlled exchange of molecules through the transcellular pathways are carrier mediated transport, transcytosis and lipophilic diffusion.

FIGRUE 2 : THIS PICTURE SHOWS TIGHT JUNCTION BETWEEN ENDOTHELIAL CELL OF INNER RETINAL BARRIER.



DISTRUPTION OF INNER BRB IN DIABETIC

Protein Kinase C (PKC)

In the diabetic, higher concentration of diacylglycerol which stimulate PKC to translocate into plasmamembrane and activate the acquire phosphorylation activities. High blood glucose induced the activation of PKC is associated with the diabetic retinopathy pathology. The actual mechanism of PKC induced vasculopathy in diabetic

retinopathy still remains unclear.PKC, especillay β-isoform is considered as a key indicator of VEGF induced BRB disruption and retinal vasculopathy. Recently,it is reported that PKCδ is also decrease the expression of the endothelial tight junction (ZO-1, 2) and also vascular hyperpermeability in diabetic retina .In addition,PKC activate occludin phosphorylation is shown to participate in the VEGF induced vascular leakage.

Some investigations also suggest that nitric oxide (NO) pathway is a potential downstream target of PKC induced vascular leakage.

Advanced Glycation Endproducts (AGEs)

Hyperglycemic environment for long-term exposure results in a non-enzymatic reaction of protein, lipid and nucleic acid to form a irreversible products called AGEs. The clinical evidence of AGEs is well demonstrated in diabetic patient.

In type 1 diabetic patients, glycated collagen and carboxymethyllysine (a kind of AGEs) in skin showed correlation with the progression of diabetic retinopathy.

Hydroimidazolone, one of the mostprominent AGEs,level in vitreous is reported to be high in type 2 diabetic patient. AGE –RAGE (receptor of AGE) interaction result in toxic effect to pericyte which is

mediated by ROS production through AGE-RAGE interaction leads to oxidation of DNA, membrane lipid protein peroxidation and apoptosis pericyte cells.

In addition, AGEs stimulate the expression of growth factors from pericyte and also inflammatory reactions which results in disturbance of BRB function.

PATHOPHYSIOLOGY

The real mechanism of diabetic retinopathy is not known yet.still many theories have been proposed.

Sorbital, a byproduct of aldose reductase,usually not crosses cell wall. In diabetic mellitus concentration of aldose reductase high in retinal pericytes.high concentration of sorbitol generate osmotic gradient that leads to electrolyte imbalance and eventually cell damage. A polymorphism near the transcription site of aldose reductase gene associated with early onset development of diabetic retinopathy in type 2 diabetic patients.but, clinical trial failed to prove the efficacy of aldose reductase inhibitor in preventing development of diabetic retinopathy.

Alternatively, another theory postulates that vasoproliferative factors released by the retina,retinal vessels,retinal pigment epithelium responsible for neovascularization.

Experimental models suggest that neovascularization is mediated in part by the interaction between insulin-like growth factor (IGF-1) and vascular endothelial growth factor (VEGF).Animal study showed IGF-1 antagonist reduced the incident of neovascularization.this is clinically evident by worsening of diabetic retinopathy after insulin therapy. Insulin increases serum IGF-1 while Pituitary injury decreases IGF-1 which reverse the condition.Recently, studies more focused on VEGF role in neovascularization. It has been demonstrated that VEGF more concentrated in vitreous in case of PDR than those with NPDR, and intensity of immunostaining for VEGF is proportional to the severity of retinopathy. This theory become more evident because VEGF inhibitors have been successful in controlling hypoxia-induced neovascularization in certain animal models.

Recently, erythropoietin may also contributes to progression of retinopathy. The local concentration of erythropoietin has been found to be much higher in patients with active proliferative retinopathy.this factor has been more correlated than VEGF because erythropoietin inhibitors slowed down the proliferation of endothelium and regress the retinal neovascularization.

Other vasoactive factors includes basic fibroblast growth factor (bFGF) and hepatocyte growth factor.concentration of this factors

increased in vitreous in PDR. these factors are strongly correlated with inducing factors of neovascularization to ischemia.

Hyperglycemia impairs autoregulation of retinal blood flow. so, In diabetic even minimal increase in blood volume can cause shearing force over retinal blood vessel and results in vasoactive factors release.

Genetic factors also susceptible for retinopathy. It is evident by first degree relatives with retinopathy have three time risk of developing severe retinopathy.some study suggesting mechanism for this could be platelet abnormality or hyperviscosity leads to focal attenuation and ischemia result in neovascularization.

ANATOMICAL AND FUNCTIONAL CHANGES IN DR

Structural changes in the retinal capillary wall includes

- Pericyte loss
- Endothelial cell loss
- Basement membrane thickening
- Endothelial cell dysfunction.

All these structural abnormalities results in loss of autoregulation of retinal blood vessels, leakage of capillaries into the extracellular space of the retina.

The rheological changes results from hyperglycaemia include

- Increase in fibrinogen α2 globulins and decrease in serum albumin levels in plasma results in decreasing fibrinolysis and increased viscosity.
- Inability of red blood cells to deform.
- Platelet aggregation.

Both structural changes of blood vessels and rheological changes results in thrombosis and closure of the retinal capillaries results in capillary non perfusion area. These ischemic area of retina stimulate the production of vasoproliferative substances results in development of new vessel formation.

Clinical features

- Microaneurysms
- Intraretinal hemorrhages
- Hard exudates
- Cotton wool spots (soft exudates)
- Venous beading
- Intraretinal microvascular abnormalities (IRMAs)
- New vessels (NVD, NVE)

Microaneurysms

- Earliest lesion detected clinically
- Loss of intramural pericytes wrap and decrease in pericyte and endothelial ratio & result in weakening and outpouching of vessel wall.
- 50-60 microns thick
- New MA – dark red in color
- Old MA – yellow to white in color due to hyalinization.
- In FFA ,it appears as bright hyper fluorescent dots.
- Life span – months to years

FIGURE 3 : MODERATE NPDR WITH EXUDATES AND HEMORRHAGES

Intraretinal hemorrhages

- MA, decompensated capillaries, IRMA may cause intra retinal hemorrhage.
- Superficial haemorrhage are flame shaped due to arrangement of Nerve fiber layer
- dot & blot pattern seen in deep haemorrhage located in the inner deeper layers
- FFA shows blocked fluorescence

Hard exudates

- Vascular leakage in to neuronal element gets absorbed by surrounding intact blood vessels leaving behind break down lipid products.
- yellow material with discrete margin
- Seen in Outer plexiform layer of the retina
- Circinate pattern seen around focal leaking MA/capillaries
- Course -absorbed by phagocytic action of macrophages on later phase.

Cotton wool spot

- 'Soft exudate'
- Micro infarction and ischemia of Nerve Fibre Layer.

- Coagulative necrosis of nerve fibre results in stasis of axoplasmic flow.
- Fluffy white in appearance with ill defined margins.
- FFA - Hyperfluorescent due to leakage and staining.

Intraretinal microvascular abnormalities - IRMAs

- Suspected new vessels between arterioles and venules
- Dilated pre-existing capillaries
- Seen in areas of capillary non perfusion
- Act as shunt vessels between arterioles and venules
- Adjacent to ishchemic retina
- Usually Budding from venous end
- Multiple IRMAs indicate a state of hypoxic region and progression to a high risk of PDR (>50%)
- FFA - larger than normal capillaries calliper

  - Usually do not leakage from IRMA.

  - Donot cross any major blood vessel

FIGURE 4: VERY SEVERE NPDR WITH VENOUS ABNORMALITIES

Venous changes

- Venous beading, looping or sausage like segmentation
- Seen in areas of focal ischemic retina
- Denotes of severe hypoxic state of the retina(40- 80% risk of PDR)
- FFA – seen adjacent to areas of Capillary drop out area.

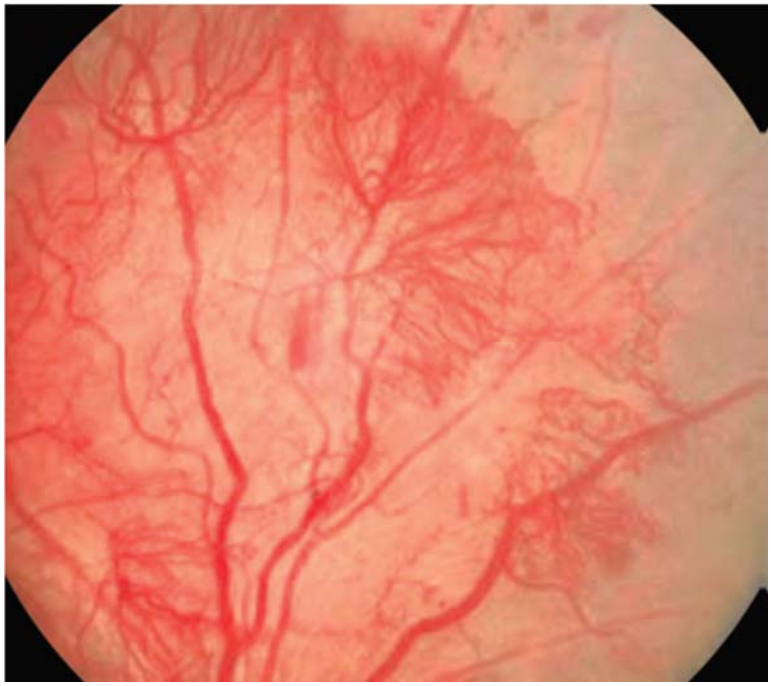
New vessels

- Derived from Primitive mesenchymal element.
- New vessel formation contain only endothelial component, pericyte is abscent results in leakage.

- Fibrocyte component – fibroglial tissue growth along with vessels form fibrovascular band
- Usually situated posterior to the equator

  Shape – fronds, compact spherules, stringy pattern etc

FIGURE 5: PDR WITH NEW VESSELS



NVD

- New vessel formation on the disc or within 1 DD
- It occurs when > $1/4^{th}$ of the retina hypoxic.
- Associated with preretinal/vitreous hge
- FFA – early hyper fluorescence and profuse leakage in late phases

NVE

- NVE usually located along the major temporal arcades

Extraretinal hemorrhage

- Subhyaloid
- From NVD or NVE
- Contraction of fibrovascular band elements leads to Tractional Retinal Detachment.

ETDRS Revised modified Airlie House diabetic retinopathy classification

ETDRS level	ETDRS severity	ETDRS definition
10	No retinopathy	Diabetic retinopathy absent
20	Very mild NPDR	Microaneurysms only
35	Mild NPDR	Hard exudates, cotton-wool spots, and/or mild retinal hemorrhages
43	Moderate NPDR	43A:retinal hemorrhages moderate in 4 quadrant or severe in 1 quadrant 43B:mild IRMA in 1 to 3 quadrants
47	Moderate NPDR	47A:both level 43 characteristics 47B:mild IRMA in 4 quadrants

ETDRS level	ETDRS severity	ETDRS definition
		47C:severe retinal hemorrhage in two to three quadrants 47D:venous beading in one quadrant"
53A-D	Severe NPDR	53A:≥2 level 47 characteristics 53B:severe retinal hemorrhages in 4 53C:moderate to severe IRMA in at least 1 quadrant 53D:venous beading in at least 2 quadrants"
53E	Very severe NPDR	≥2 level 53A-D characteristics
61	Mild PDR	NVE <0.5 disk area in 1 or more quadrants
65	Moderate PDR	65A:NVE≥ 0.5 disk area in 1 or more quadrants 65B:NVD< 0.25-0.33 disk area
71 and 75	High-risk PDR	NVD ≥ 65B, or NVD < 65B or NVE ≥ 0.5 disk area plus VH or PRH, or VH or PRH obscuring ≥ 1 disk area
81 and 85	Advanced PDR	Fundus partially obscured by VH and either new vessels ungradable or retina detached at the center of the macula

DR classified as follows:

Grade 0: absence of DR (no DR), corresponding to level 1 of the abbreviated version of the Modified Airlie House classification (23);

Grade 1: background DR (BDR), comprising levels 2, 3, and 4;

Grade 2: pre-proliferative DR (PPDR), corresponding to level 5;

Grade 3: proliferative DR (PDR), equivalent to level 6.

NEURONAL DAMAGE IN DIABETIC RETINOPATHY

Neurodegeneration

A nerve damage in diabetic neuropathy begins immediately after the onset of diabetes. Several investications play a role in screening purpose such as multifocal electroretinography (ERG), flash ERG, color vision, contrast sensitivity and short-wavelength automated perimetry.

Retinal glial cells play a vital role in maintaining normal function of retina. In diabetic, upregulation of (GFAP) glial fibrillary acidic protein in glial cells and selective thinning of ganglion cells and inner plexiform layer.this results in altered potassium siphoning,GABA uptake, glutamate excitotoxicity in glial cells leads to expression of angiogenic factors.

Apoptosis

Diabetes increasing the frequency of apoptosis by inducing proinflammatory cytokine (IL-1β) and caspase-1/IL-1β signaling pathways results in chronic loss of retinal neurons.it is demonstrated by presence of pyknotic bodies in histological section of diabetic retina.

Several studies suggested that the expression of proapoptotic Protein, Bax (Bcl-2 associate X protein) is associated with degenerative diseases which is increased in diabetic retina. The pro-apoptotic transcription factor Forkhead box O1 (FOXO1) activates the pericyte apoptosis through the involvement of TNF-α and AGE is the possible mechanism for apoptosis.

Glutamate excitotoxicity

Glutamate is the excitatory neurotransmitter in the retina, but it becomes neurotoxic when it is present in excessive amounts. Extracellular glutamate is transported into mullers cells by glutamate transporters

↓

Glutamine synthase

Glutamine (non toxic amino acid)

↓

In diabetic, inability of Muller cells to pump out excess glutamate, excess glutamate in post synaptic neurons activate

- amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors
- N-methyl-D-aspartate (NMDA)

↓

Influx of calcium and sodium in to the cells

↓

Generation of AGE and advanced lipoxidation end product

↓

Defective mitochondrial respiration

↓

Formation of free radicals

↓

Neurotoxicity

↓

Neurodegeneration

ROLE OF NEUROTROPHIC FACTORS

Brain derived neurotrophic factors (BDNF)

- It enhances insulin sensitivity by activating several signaling pathway including phosphatidylinositol-3 kinase/Akt.

- Biomarker of insulin resistance.
- In hypoxic condition, BDNF enhances mullers cells to take up increased glutamate and upregulate glutamine synthetase.
- Combine with ciliary neurotrophic factor (CNTF), it rescue photoreceptors in retinal explants and have neuroprotective effect.

Nerve Growth Factor (NGF)

- Potent neurotrophic factor, which contributes for retinal inflammation.
- Potent angiogenic factor in PDR.

Basic Fibroblast Growth Factor (bFGF)

- Role in survival and maturation of both glial cells and neurons.
- Mediator for regeneration after neural injury
- Potent angiogenic factor in pathogenesis of neovascularization.

Glial cell line-derived neurotrophic factor (GDNF)

- Transforming growthfactor-β (TGF-β)-related neurotrophic factor family
- It rescue photoreceptor and muller glial cells during rtinal degeneration.

MANAGEMENT OF DIABETIC RETINOPATHY

LASER

Light amplification by stimulated emission of radiation-when electron shift from higher energy level to lower energy level radiation is emitted.

Characteristics of a LASER

- Monochromatic light
- Spatial coherence
- High density of electrons

Laser effects on the eye

- Photocoagulation
- Photovapourization
- Photoablation
- Photoradiation
- Photodistruption

PHOTOCOAGULATION

When light energy is applied to targeted tissue, the light energy is converted to heat energy. So, temperature at treated tissue raises from 37º up to 50ºc result in denaturation of tissue protein and coagulation of the absorbant tissue.

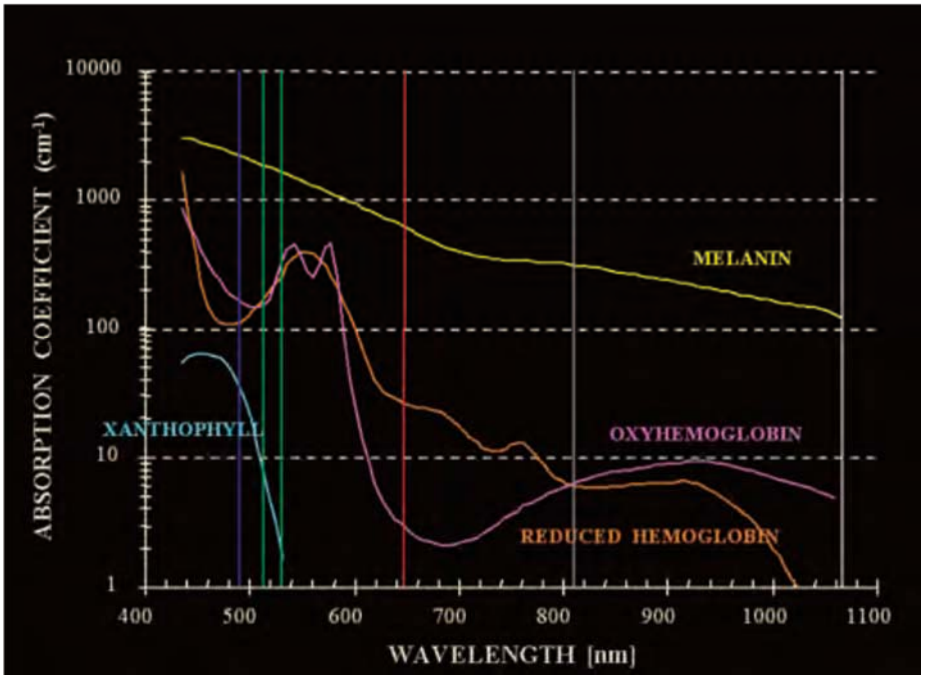
Melanin pigment absorbe light spectrum between 400 to 700nm which is principle absorber of light in photocoagulation of trabecular meshwork and co absorber of light in retinal pigment epithelium and choroid.

Xanthophyll pigment more concentrated in the inner and outer plexiform layers of retina of the macular area.it absorbs blue light maximally and green light poorly.

Hemoglobin absorbs blue green and yellow light and red light poorly. These pigment absorbe shorter wavelength easily and longer wavelength lights are unabsorbed.

FIGURE 6

Plot of the absorption coefficient as a functionof wavelength for the most importantocular chromophores: melanin, oxygenated hemoglobin, deoxygenated (reduced) hemoglobin, and xanthophyll. The vertical lines correspond tothe laser wavelengths.



LASERS COMMONLY USED IN PHOTOCOAGULATION

1. CW GREEN ARGON LASER(514.5nm)

It is absorbed selectively by the RPE, hemoglobin pigments, choriocapillries, layers of rods and cones and at the outer and inner nuclear layers.It coagulates from choriocapillaries to inner nuclear layer of retina.

2. FREQUENCY DOUBLED Nd: YAG LASER(532nm)

It is solid state and diode pumped CW laser and mainly absorbed by hemoglobin and the melanin present in retinal pigment epithelium and trabecular meshwork.it coagulated from choriocapillaries to outer nuclear layer of the retina.

3. KRYPTON RED LASER (647nm)

It is readily absorbed by melanin granules but not absorbed by the hemoglobin and xanthophylls. So it is used for macular photocoagulation.since,it is not absorbed by retinal vasculature it can penetrate deeper to coagulate choriocapillaries and Choroids.

4. DIODE LASER (810 nm)

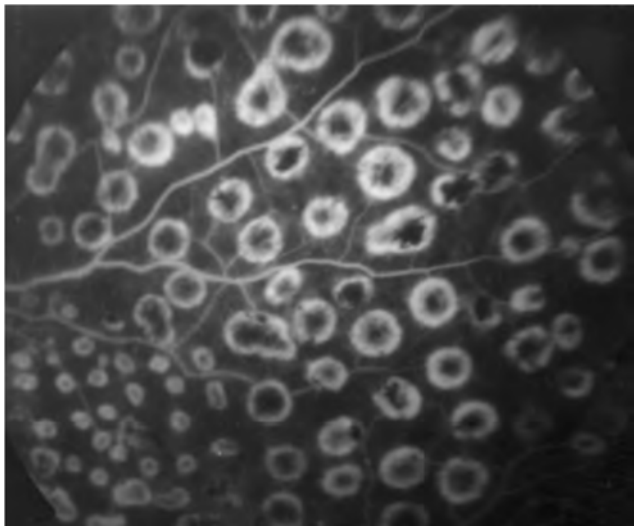
It is the most important semiconductor laser GaAs.it is very difficult to coagulate microaneurysm directly because it is very poorly absorbed by hemoglobin.

GRADING OF PHOTOCOAGULATION LESIONS

- GRADE 1/ LIGHT -Barely visible blanching of retinal pigment epithelium
- GRADE 2/MILD - Hazy, faint white retinal coagulation
- GRADE3/MODERATE –Opaque ,dirty white retinal coagulation
- GRADE4/HEAVY -Dense white, chalky retinal coagulation

FIGURE 7: MODERATE NPDR WITH POST PRP STATUS

FIGURE 8: FFA –SCATTER PRP IN THE PERIPHERY



FOCUSING OF LASER BEAM

All lasers except xenon arc emit monochromatic rays .so, all laser beam except xenon arc should be focused in a fine point without chromatic aberration.

- The properly focused laser beam in an eye without any opacities in the refracting mediums should be in circular with clear cut margin.
- In incorrect focusing, beam should be oval with blurred margin.
- Large wedge shaped deficit indicate cortical cataracts.
- Elongated and irregular outlines indicates astigmatism.
- Round hazy focus with irregular outline seen in diffuse haziness of ocular media.
- In vitreous opacity focusing beam presented with large irregular deficit.

PHOTOVAPOURIZATION

Laser irradiation can raises tissue temperature can reach the boiling point of water and sudden fast expansion of water vapour results in tissue distruption.it is usually accompanied with photocoagulation.

PHOTOABLATION

In photocoagulation, temperature raise does not take place in the shorter wavelengths of the ultraviolet spectrum. At the site of impact, the

tissue simply disappears without any charring and temperature rise. Surface of target tissue can be precisely removed in photoablation.

PHOTORADIATION

Hematoporphyrin derivative is selectively taken up by metabolically active tumor tissue.when this photosensitized tisuue is exposed to 630nm red lights from a dye laser, producing cytotoxic singlet oxygen and tissue distruction.

Verteporfin mainly accumulates in choroidal neovascular membrane.In photodynamic therapy the choroidal neovascular membrane is subjected to laser emission from diode (689nm) with resultant occlusion and thrombosis of the neovascular tissue.

PHOTODISRUPTION

In photodistruption, temperature of treated localized microscopic area of tissue is increased from 37ºC to 15000ºC.On optical breakdown at the desired site, electron are stripped from the atoms of target tissue producing acousting shock wave leads to mechanical tearing of the tisuue microscopically.

PAN RETINAL PHOTOCOAGULATION

The Carl Zeiss laboratory developed Xenon Arc Laser in 1950s which was used in early days. The Argon laser was discovered by William Bridges in 1964. In 1976, Early Treatment Diabetic Retinopathy Study published that extensive application of laser in diabetic retinopathy can reduce 50% risk of visual loss in, atleast in the following of 2 years and also ETDRS demonstrated that photocoagulation reduces the risk of visual loss in patient with clinically significant macular edema.

Pan retinal photocoagulation is done in systemically stable patient, Only when the blood sugar and serum lipid level are well controlled.

- According to diabetic retinopathy study, Indications for panretinal photocoagulation are
- Moderate or severe Neovascularization of disc(NVD)(atleast 1/4th -1/3rd disc area in extent)
- Mild NVD, if associated with preretinal or vitreous haemorrhage.
- Neovascularization elsewhere(NVE)(atleast ½ disc area in extent),if associated with preretinal or vitreous haemorrhage.
- Rubeosis of iris or anterior chamber angle.

- Eye with feature of extensive retinal ischemia i.e,capillary non perfusion area,retinal hemorrhage,soft exudates.
- Patients with severe proliferative diabetic retinopathy in other eye.
- High risk proliferative stage.
- In pregnancy or after renal transplantation in patients with severe pre-proliferative diabetic retinopathy or proliferative diabetic retinopathy even without high risk characteristics.

CONTRAINDICATION

- Eyes with mild to moderate non-proliferative diabetic retinopathy.
- Relative contraindication-If proliferative diabetic retinopathy coexists with clinically significant macular edema, either focal or grid laser treatment of CSME is done first followed by PRP after 6 weeks later.

PROCEDURE

- Explain about the procedure to patient and get the informed consent.
- Pupil should be maximally dilated with tropicamide (1%) and phenylepinephrine(5%).

- 1% apraclonidine or 0.2% brimondine tartate eye drop applied one hour prior to the procedure to prevent post laser intraocular pressure spike.
- 0.5% topical proparacain applied few minutes before the procedure. peribulbar injection of lignocain required in nystagmus and
- Uncooperative patient.
- Make the patient to sit comfortably on revolving stool.
- Apply head strap and adjust fixation target.
- Insert appropriate Laser contact lens.
- Room should be darkly illuminated.
- Adjust slit lamp beam PRP can be applied through 3 deliver system.

LASER DELIVERY

1.Slit-lamp Biomicroscope

2.Laser Indirect Ophthalmoscope

3.Intraoperative Laser Endoscope

LASER CONTACT LENS

LENS	IMAGE MAGNIFICATION	LASER SPOT MAGNIIFICATION FACTOR	FIELD OF VIEW
Goldmann 3-mirror	0.93x	1.08x	140º
Mainster widefield	0.68x	1.5x	118-127º
Mainster PRP 165	0.51x	1.96x	165-180º
Volk quadraspheric	0.51x	1.97x	120-144º
Volk Supra Quad	0.50x	2.00x	160-165º

- PRP is usually divided over 3 sessions with 1-2 weeks interval between the sessions
- The diabetic retinopathy study protocol recommended 800-1600 burns in PRP.however, 1800-2200 burns are often reported.
- It extends from 500µm nasal to the optic disc margin 2DD (300µm) temporal to, above and below the macular center, just within the vascular arcade and extending peripherally to or beyond the equator.
- Burns along location of ciliary nerves are usually painful.
- During PRP, vitreous hemorrhage may occur from new vessels and is immediately controlled by pressing over the eye with the contact lens.

- In patient with cataract, if the media sufficientely clear to permit photocoagulation, should have PRP prior to cataract extraction. If ocular media is very dense then cataract extraction is followed by PRP.
- Photocoagulation over major vessels, vortex veins, retinal hemorrhages and chorioretinal scars, papillomacular buddle should be avoided.
- Superimposition and overlapping burns should be avoided.

POST LASER ADVICE

- Topical cycloplegic
- Topical steroid 3-4 times daily for atleast 3 adys after each session.
- Tablet acetazolamide 250mg –if IOP spike is observed in treated eye.

POST LASER FOLLOW UP

1st follow up - 3 or 4 weeks after 3rd or final PRP session.

2nd follow up - 3 or 4 weeks interval.

3rd follow up - 3or 4 weeks interval.

Subsequent follow up- 3 months interval.

COMPLICATION OF PANRETINAL PHOTOCOAGULATION

1. MACULAR EDEMA

It is reversible medium term complication but it may cause rapid irreversible progression of the maculopathy commonly in type 2 diabetic patients especially in pre-existing maculopathy.

This is due break in blood retinal barrier which is formed by zonnula occludens of endothelium in retinal capillaries and retinal pigment epithelial cells.RPE cells form tight junction by zonula occludents and zona adherens.

Pan retinal photocoagulation causes damage to RPE and bruchs membrane results in leakage and macular edema.

2. VISUAL FIELD DEFECT

Visual field loss following panretinal photocoagulation depends on intensity and number of laser burns. Repeated burns over the same spot leads to severe damage to focal retina results in scotoma .full threshold PRP uncommonly produce visual field loss, but following fill in PRP results in peripheral field loss due to nerve fibre layer damage.

3. VITROUS HEAMORRHAGE

When PRP is not enough to halt neovascularization then traction of fibrovascular band results in vitreous heamorrhage or tractinal retinal detachment or retinal distortion leads to sudden severe visual loss.

4. CHOROIDAL EFFUSION

It is most commonly after extensive dose full scatter PRP due inflammation. It is associated with myopic shift of about 4D and shallowing of anterior chamber. It can be prevented by doing PRP in multiple sessions. PRP is avoided in uremic patients.

5. PHOTOCHEMICAL DAMAGE TO MACULA

In the absence of macular edema, patient lose one or more line in snellen's chart may be the result of photochemical damage to macula due to light reflection from the laser.

6. NYCTALOPIA

PRP can damage rod photoreceptors with increasing scotopic thresholds. Patients may develop prolonged adaptation time, changing luminance. Also, poor hue discrimination after PRP due cone destruction.

7. ACCOMMODATIVE DEFECTS

Photocoagulation over horizontal meridian can damage long ciliary nerve which is not covered by retinal pigment epithelium.it also result in severe pain.

8. CONSECUTIVE OPTIC ATROPHY

Laser axotomy lead to calcium wave dependent calpine activation leads to depolymerization of microtubules and disorganization of axonal plasmalemma results in apoptosis of retinal ganglion cell.

Apoptotic retinal ganglion cell releases factors from dying neurons or glia which affect anterograde axonal transport function and Wallerian degeneration of unmyelinated retinal ganglion cell axon results in consecutive optic atrophy

- Clinical features-Vision <CFCF
- Pupil-Relative Afferent papillary Defect
- Kestenbaum index<6
- Waxy pallor disc
- Defective colour vision and Contrast sensitivity

9. CORNEAL BURNS

Inadvertent burning of papillary margin, non targeted area of retina.

10. POSTERIOR VITREOUS DETACHMENT

11. INCREASED INTRAOCULAR PRESSURE

- It may be due to Angle closure Glaucoma results from choroidal detachment
- Pigment Dispersion
- Steroid induced glaucoma
- Rubeosis iridis

PATTERN SCANNING LASER

Recently, the traditional laser parameters have been modified in order to minimize the side effects while retaining its therapeutic effect. Pattern scanning laser retinal photocoagulation introduced recently, which applied laser in a patterns of 4 to 56 burns in less than 1 second with shorter pulse durations using a scanning laser automatically. Several clinical units are currently available, including

- PASCAL (Topcon Corp, Santa Clara, CA, USA),
- Visulas 532s VITE (Carl Zeiss Meditec, Jena, Germany), and
- Model of Quantel in France

These systems delivers well-aligned rows of retinal lesions in a shorter duration. On examination of retinal photocoagulation have showed that 10 to 20 ms exposures can able to produce retinal lesions of all four clinical grades according to increasing power. And also, shorter duration of pulse energy result in selective lesion localization, as compared to conventional laser technique where uses 100 ms duration. Patterned scanning laser uses parameters of

- 532 nm wavelength,
- 20 ms duration, 200 μm,
- Power- 300 to 750 mW.

In conventional PRP, the appearance of grayish-white lesion that is formed due to denaturation and photocoagulation of the retina by thermal energy is the end point of laser treatment seen opthalmoscopically. Recent studies has showed, however, that retinal burnt lesions might not be permanent ,as in less intense and small burns the outer retina can fill the damaged areas in animal models. light PRP also named as minimum intensity photocoagulation (MIP) .Several reports have indicated that these approaches such as minimum intensity photocoagulation (MIP) and subvisible treatment using micropulse photocoagulation may have an equivalent efficacy over conventional PRP in regression of high-risk PDR. Small studies suggested that MIP is associated with only fewer complications and less treatment sessions.Therefore, these approaches could give the therapeutic benefit as much as of conventional therapy without its side effects

NEW LASER DELIVERY SYSTEM

Subthreshold Treatment

In order to reduce complication and better outcome of laser therapy, possible modifications have been done inn laser intensity and duration, but with similar efficacy. These are termed as minimum intensity photocoagulation. :

- Selective retinal therapy (SRT)
- Transpupillary thermotherapy (TTT)
- Subvisible diode micropulse (SDM) photocoagulation

Selective Retinal Therapy

In this pulse duration is decreased to microsecond domain selectively over RPE. therefore, microsecond pulse laser below thermal relaxing time of melanosomes destroys only RPE leaving photoreceptors, ganglion cells and nerve fibre. It uses

- Argon laser
- Pulses at 514 nm over 5 µs
- Repetition rate of 500 hz

Transpupillary Thermotherapy

- It uses near-infrared laser (NIR – 810 nm) .
- Long exposures time (60 s).
- Large spot size (1.2–3 mm).
- Low irradiance (~10 W/cm^2).

Subvisible Diode Micropulse Photocoagulation

This technique uses near infrared laser (810nm) which is not absorbed by hemoglobin and photoreceptors, thus more laser energy are selectively absorbed by melanin pigment of RPE and choroid. Hence, short pulse and small size laser is efficient to cause destruction of RPE.hyperthermia produced by this technique not

- Exceed cytotoxicity.
- Near infrared laser (810nm).
- 100 μs
- Separated by 50-150 μs.

FIGURE 9

Pictures showing FDA-approved units using different wavelengths and micropulsing energy availability. By using this ultrashort pulse (micro- and nanosecond) technology selectively damage the RPE and spares the sorrounding retina

MECHANISM OF SUBLETHAL LASER

After several studies regarding mechanism of action of laser therapy, still it requires active investigation.Many studies concentrated on local cytokines which is released during laser therapy, thought to be playing important roles, including, pigment epithelial-derived factor (PEDF), VEGF, tissue inhibitor of matrix metalloproteinases (TIMP) and matrix metalloproteinases (MMP).

It has been shown that the direct thermal injury or oxygen reperfusion during laser treatment results in an increased free-radical activity, and it has been shown that laser causes a surge in free radicals.The activity of transforming growth factor-beta 2 (TGF-β2) and MMP (specifically, MMP-9 and alpha2M) have also been increased dramatically after laser application.

Angiostatin has been shown to modulate the effects of laser.Recently,In animal experiment have found that photoreceptors secrete growth factors in hypoxic conditions that results in angiogenesis and increased vascular permeability.

Heat shock proteins (HSPs) are indicators of cellular response to stress in retina. HSPs helps as chaperone proteins in the refolding of denatured proteins They also inhibit misfolded protein aggregation, direct

target proteins for destruction or repair, and stabilizing the cytoskeleton for maintain cell structure.

Commonly, HSPs are expressed in low levels at baseline, but increased expression seen in condition of thermal, ischemic, and oxidative stress. HSPs are considered as a significant element in required for thermotolerance in heated tissue.

HSPs also play an important role in the apoptotic and inflammatory pathways. They act on both caspase-dependent and caspase-independent cascades in different tissue types, including neuronal ganglion cells. HSP70 prevent mitochondrial cytochrome c release and also upregulates Bcl-2, an anti-apoptotic protein.

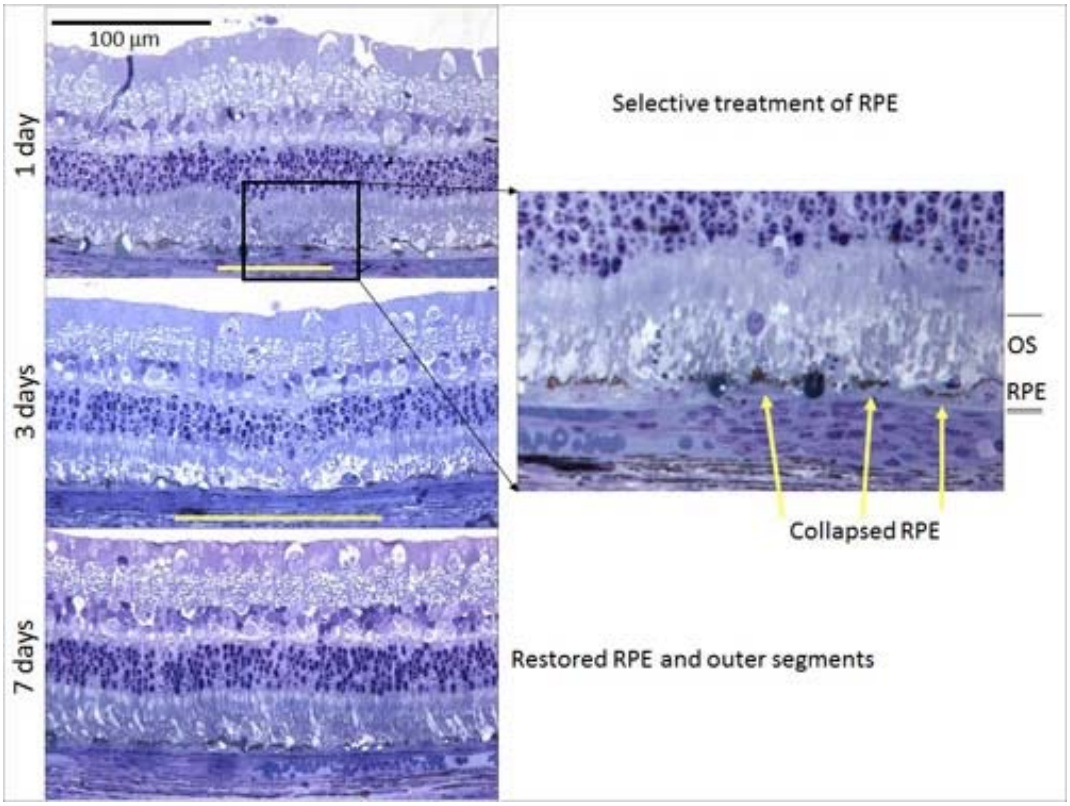
HSP70, 70 kD in size, which prevents the formation of caspase-dependent central complex apoptosis, suppress the caspase-3 activation, and interferes with apoptosis inducing factor (AIF) in caspase-independent pathway. HSP interacts with a transcription factor, NFkB, which is associated with genes involved in inflammation, and it also inhibit IkB to decrease TNF-a.

HSP response has been demonstrated in the choroid and retina after laser treatment in rabbit and rodent models. It has been found that in mice laser treatment that damage RPE at half the threshold power (100

ms, 532 nm, 400 µm diameter) upregulate the transcription of HSP70, an indication of cellular response to sublethal thermal stress.

FIGURE 10

THIS PICTURE SHOWS FOCAL ATROPHY OF RPE AFTER PRP.



PHARMACOLOGICAL MANAGEMENT

VEGF Inhibition

- VEGF is a ligand for two tyrosine kinases receptors, VEGFR-1 and
- VEGFR-2, that act through downstream signaling cascades.
- Promote angiogenesis.
- VEGF is expressed in many cell types, including pericytes, endothelial cells, glial cells, neurons, and the RPE

Hypoxia

↓

Capillary dropout

↓

Upregulation of VEGF

↓

Phosphorylation of endothelial constituent proteins

↓

Disruption of tight junctions of adjacent endothelium

↓

Formation of transendothelial pores and fenestrations in the endothelial cell membrane

↓

Enhanced vascular permeability

- VEGF also a mediator of the inflammatory change

Elevated level of VEGF

↓

Upregulation of ICAM-1

↓

Fas-FasL-mediated apoptosis

↓

Retinal leukostasis and endothelial cell damage

↓

Breakdown of blood retinal barrier

Bevacizumab

- Humanized antibody for all isoforms of VEGF A.
- Decrease endothelial cell permeability and nitric oxide production, thereby reducing vascular leakage.
- 0.05mL injection containing 1.25 mg of bevacizumab.

Ranibizumab

- Engineered Fab fragment
- Reacts with all VEGF isoforms.
- 0.5-mg ranibizumab in 0.01 ml.

Pegaptanib

- An anti vascular endothelial growth factor (anti-VEGF) RNA aptamer.
- 0.3 mg, 1 mg, or 3 mg

Inhibition of PKC-β

- Ruboxistaurin is an orally administered inhibitor specific for PKC-β.
- Both orally and intravitreally ruboxistaurin significantly inhibits increased retinal permeability.

- GF109203X, reverse BRB breakdown, resulting in controlled retinal permeability

Anti-leukocyte adhesion agents

- Leukocyte adhesion to the diabetic retinal vasculature is the early event in the pathogenesis of DR, resulting in breakdown of the blood-retinal barrier and capillary nonperfusion.
- Sulphonylurea gliclazide decreases the adhesion of neutrophils to endothelial cells and leukocyte entrapment in the retinal microcirculation.
- Gliclazide, selectively beneficial for preventing development of DR
- Nipradilola, topical antiglaucoma αβ-blocker significantly reduces retinal leukostasis in the retinal microcirculation.

VISUAL EVOKED POTENTIAL

History

- In 1934, Adrian, Matthew noticed stimulation of retina by light produces potential changes in the occipital EEG.
- In 1961, Hirsch taken EEG record from the occipital lobe.
- Later, Spehlmann first used checkerboard pattern for stimulation on retina.

Types of VEP

1. Monocular pattern reversal (most common).
2. Flash visual evoked potential.
3. Multifocal visual evoked potential.
4. Binocular visual evoked potential.
5. Chromatic visual evoked potential.
6. Hemi field visual evoked potential.
7. Sweep visual evoked potential.
8. Motion visual evoked potential.
9. LED Goggle visual evoked potential.
10. Multichannel visual evoked potential.
11. Multifrequency visual evoked potential.
12. Steady state VEP.
13. Stereo elicited VEP.

- Visual evoked potential measures the electrophysiological responses of nervous system to visual stimuli.
- It measures strength and speed of visual stimulation of the cortex objectively.
- VEP is the EEG records taken from the occipital cortex when stimuli the retina by light.

- VEP is an indicator of the integrity of the visual conduction pathway, includes the opticnerve, opticchiasma, optictract, lateral geniculate body, optic radiation and visual cortex.
- Abnormalities in VEP denote a nonselective functional neuronal loss.

Prerequisites

- Patient should be conscious, able to sit comfortable in front of the monitor of about 0.75 – 1.5meter distance.
- Patient scalp should be dry.
- Each eye tested separately.
- Spectacle correction should be given.
- Foveal fixation at the centre of the monitor.

EQUIPMENT FOR RECORDING VEP

FIGURE 11: ELECTRO ENCEPHALOGRAPHIC MACHINE

- Visual stimulus producing screen,
- Scalp electrode,
- Amplifier,
- Computer receiver and read out systems.

Types of VEP recording:

1. Flash VEP

It use calibrated intense diffuse light or continuous flahes releases 1-5 times /sec from a shutter. It is not affected by the media opacities like cataract, corneal opacities,vitreous heamorrhage.

2. Pattern VEP

Patterned visual stimulus shown on a TV screen in the form of black and white squares alternatively known as checker board pattern.

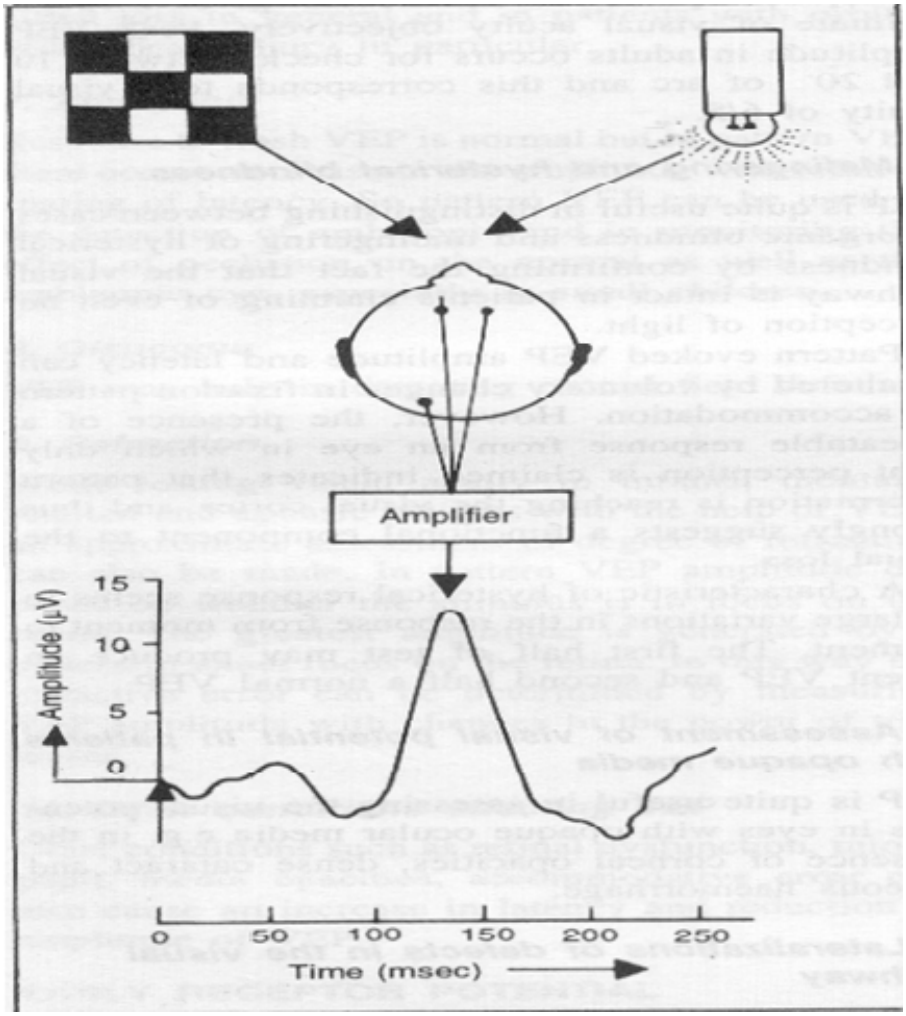
Its pattern size can be adjustable to determine the ablility of discrimination.

Two types

Pattern appearance VEP: A black and white color checker board presented in an on- off sequence.

FIGURE 12

PATTERN REVERSAL VEP



Pattern reversal VEP

In this case, the pattern of the stimulus is changed.

- The size of each check in the pattern and size of the visual field affects the VEP response.
- In Poor visual acuity patient –field subtending 10-40 degrees of arc and large check size 20mm viewed at 1meter distance.

- In better visual acuity patient-15-20 degree of arc and check size visual angle subtend at 1 min to 10 degree at 1 meter distance.

VEP electrode placement

VEP recorded from occipital scalp overlying calcarine fissure closer to brodmann's area. Recording electrodes are made either with silver chloride or gold disc.

Midoccipital(OZ) electrode is placed 2.5cm above the inion in adult on the midline.Two lateral occipital electrodes are placed 2.5cm on both side of OZ and a reference electrodes placed at Fz.

- Active electrode is placed over Midline occiput (MO)-oz
- Reference electrode over Vertex Cz
- Ground electrode over Forehead Fpz

VEP wave forms

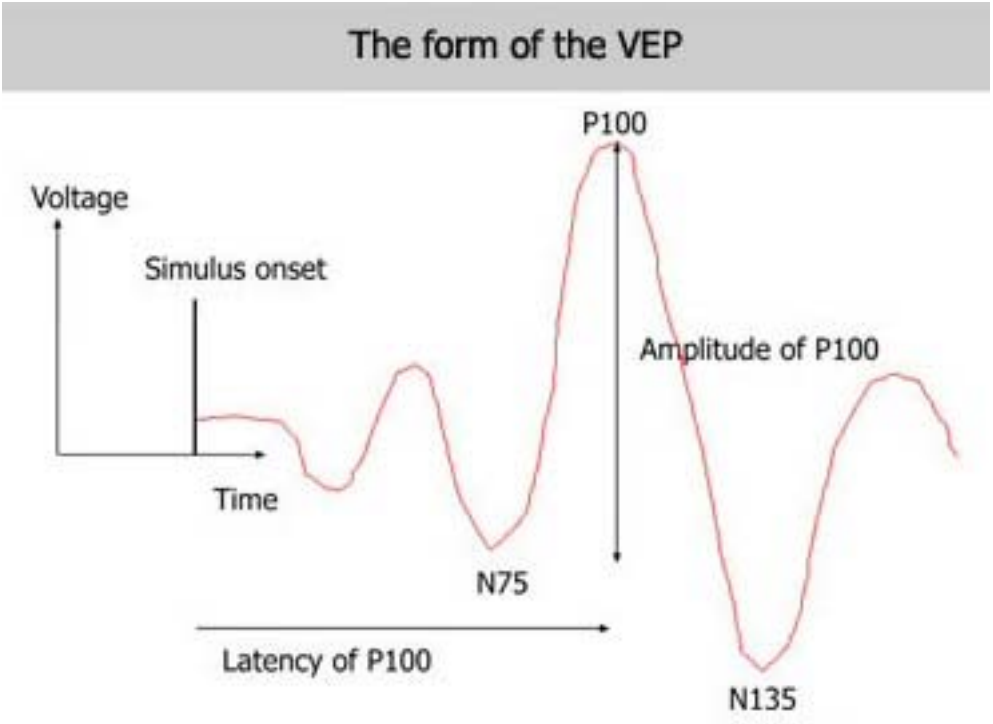
VEP shows three wave forms

Neural generators of the waves of VEP –

- N75-input from the dorsal lateral geniculate body to the striate cortex.
- P100-secondary inhibitory response at V1 /excitatory outflow to the accessory visual cortex V2 to V5.
- N145-generated from deep source in the parietal lobe.

FIGURE 13

VEP WAVE FORMS



VEP terminologies

Amplitude of VEP

- Amount of electrical energy which reaches visual cortex.
- Absence of any response when recording from multiple and lateral occipital sites, with prolonged analysis times as long as 500msec.
- Abnormally low amplitude of p100
- Abnormally high p100 interocular amplitude ratio.(range of 2:1-2.5:1 with large field stimulation)
- Primarily affected in ischemic disorders.

Latency of VEP

- Time at which electrical stimuli reaches visual cortex.(represent myelination of neuron)
- Abnormally prolonged p100 peak latency.
- Abnormally prolonged p100 interocular latency difference,with longer latency eye abnormal.
- Exceeding 2.5 or 3 standard deviation above the age matched control sample from normal population
- Seen in demyelinating disorders.

Bizzare wave forms

Both amplitude and latency is predominantly affected in compressive disorders and optic nerve injuries.

Indications

1. Optic nerve disease.
2. Traumatic optic neuropathy.
3. Infant with questionable vision.
4. Malingering and hysterical blindness.
5. Inherited retinal dystrophies.
6. Unexplained visual loss.

7. Amblyopia.
8. Vascular diseases.
9. Toxic and nutritional eye disease.
10. Refractive errors.
11. Glaucoma.
12. Suspected intracranial lesions.

Factors influencing VEP

1. **Stimulus**

In transient response, when size of the checks decreases, amplitude is increased, reaching a peak when the check square subtends at 15 arc of angle.

2. **Position of electrodes**

Position of electrode over the scalp influences the character of VEP response.

3. **Age and Sex**

Females have larger responses than males.Since female have relatively shorter visual pathway, they have slightly shorter latency response.

4. **Attention of the patient to stimulus:**

- The primary visual cortex in humans is located in fissures, not on the cortical surface of the occipital pole.
- Only about the central 10 degrees of visual field are continues on to the posterior pole of tip of the occipital cortex (stria of gennari).
- Visual information arising from the central vision is "over represented".

5. **Effect of diseases on VEP:**

1.**Optic neuritis** – Amplitude - normal,

latency - prolonged in permanent damage.

2. **Multiple sclerosis** – Delayed latency .

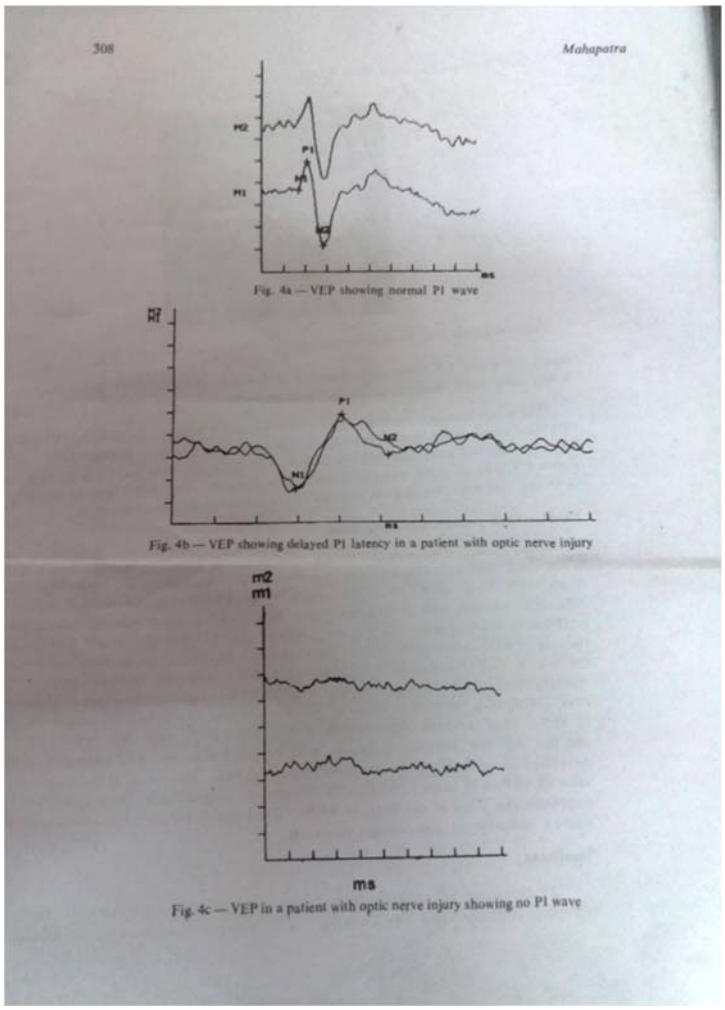
3. **Compressive optic nerve lesions-**amplitude-reduced

Latency-normal

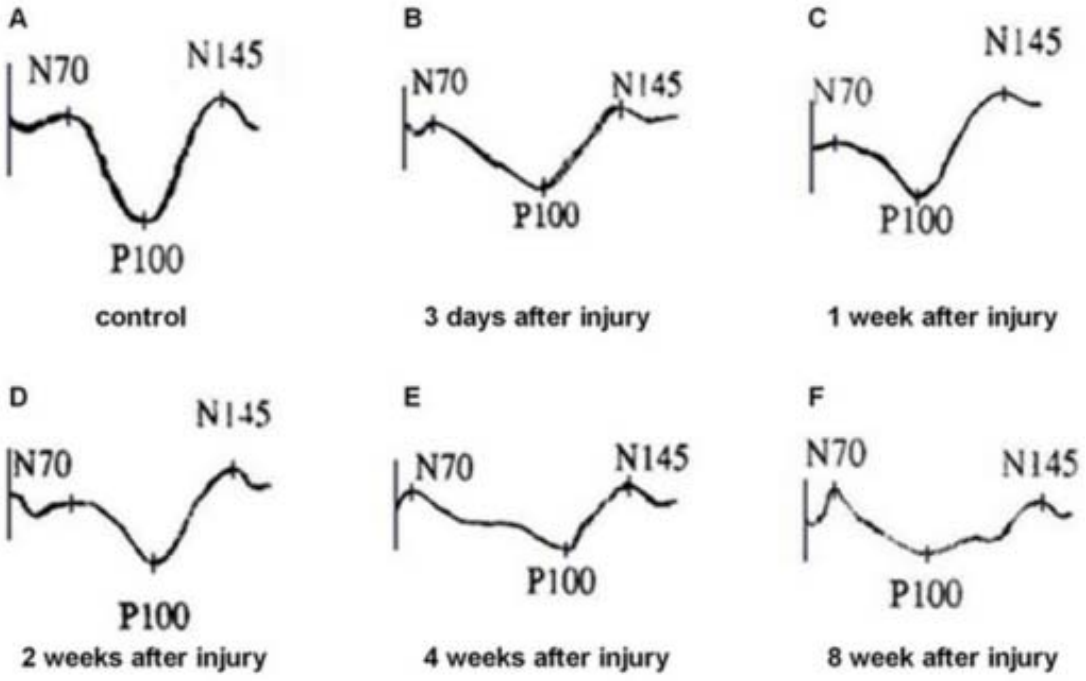
5. During orbital or neurosurgical procedures-

FIGURE 14

During neurosurgical surgery, Continuous monitoring of optic nerve function by VEP preventing inadvertent damage to optic nerve



5.**Traumatic optic nerve injuries**-delayed latency period of P100 decreased amplitude Absence of VEP wave or no response - total loss of optic nerve fibers.



Normative values of visual evoked potential:

Parameter	Range	Mean ± SD	Range	Mean ± SD
	15 checks		31 checks	
P 60 latency	50.0 - 75.0	60.9 ± 4.2	44.5 - 67.0	56.1 ± 3.5
N70 latency	63.5 - 87.5	75.5 ± 4.1	60.0 - 87.5	70.8 ± 3.7
N70 amplitude	1.0 - 18.2	5.1 ± 3.1	0.7 - 14.5	3.9 ± 2.2
P100 latency	83.5 - 107.5	98.1 ± 4.4	81.5 - 107.0	94.7 ± 5.0
P100 amplitude	1.1 - 38.1	9.9 ± 5.9	1.9 - 29.9	8.7 ± 4.7

REVIEW OF LITERATURE

Visually evoked potentials after panretinal photocoagulation in omani patients with uncontrolled diabetes mellitus.

Shenoy R, Al-Belushi H, Al-Ajmi S, Al-Nabhani SM, Ganguly SS, Bialasiewicz AA.

Abstract: AIM: To report on the changes of latency and amplitudes of the pattern VEP in patients with uncontrolled diabetes mellitus II and I before and after panretinal laser treatment.DESIGN: Single center hospital based comparative study.METHODS: One hundred eyes of patients with proliferative diabetic vitreoretinopathy, and HbA1C ≥ 10 percent were subjected to Pattern Visually Evoked Potentials (Medtronic keyopint system, Nicolet) prior to and 4 weeks after PRP. Results were compared to age-matched non-diabetic controls. Chi-Square test, and paired 't' test were used for statistical analysis.RESULTS: Preoperative mean VEP amplitude was 8.35mV±3.71, and not significantly different to the control group (mean 10.51mV±3.34) (chi square test p=1). Mean preoperative P100 latency was 106.93±7.90ms and significantly different to the control group (103.21±7.65ms) (paired t-test p=0.001). After laser treatment, VEP amplitudes decreased in 48/100 eyes (mean total 5.11mV±2.4), and P100 latency increased in 75/100 eyes (mean total

110.47±7.35ms).CONCLUSION: In this study, PRP was followed by a significant decrease in VEP amplitudes in 48 percent and increase in latency in 75 percent of eyes.

(Middle East Afr J Ophthalmol 2008 Apr;15(2):51-6)

Visual evoked potential changes in diabetes mellitus

(Avachar Kiran Narayan, Sonawane Nikhil Pandurang, Mundewadi Shafique Ahmed and Shrinivas Janardan Kashalikar)

Background: Diabetes Mellitus (DM) a metabolic disorder is the most common cause of neuropathy. Electrophysiological studies are commonly employed to detect the neuropathy. The present study was undertaken to find out the utility of visual evoked potential (VEP) as an early indicator of central neuropathy in diabetic patients. Materials & methods: The present study was carried out in 60 healthy subjects and 60 diagnosed DM patients of age group 20 to 40 years. Visual evoked potential (VEP) tests were recorded in sports physiology laboratory of Medical College on an outpatient basis, using RMS EMG.EP machine. It is to find out whether the VEP latencies are altered in diabetes or not. Result: In our study there is statistically significant increase in latencies of P100 waves of both eyes in diabetic patients as compared to control subjects ($p < 0.001$). The N75-P100 amplitude is decreased in diabetic

patients as compared to control subject but it is not statistically significant ($p > 0.05$). Conclusion: The abnormalities in the VEP response occur in diabetic patients before the development of overt retinopathy. So, VEP measurements can be used for the early diagnosis of central neuropathy to offer an early opportunity for proper management

(International Journal of Biomedical and Advance Research 2015; 6(07): 537-540)

Evaluation of Visual Outcome in Proliferative Diabetic Retinopathy After Panretinal Photocoagulation.

(Narendra Datti, Tanuja Abhilash, Balachandra)

Objectives: To evaluate maintenance of existing vision after pan retinal photocoagulation in type II diabetes with proliferative diabetic retinopathy and to assess the causes of severe visual loss after pan retinal photocoagulation (PRP). Materials and Methods: 50 eyes of 28 patients with proliferative diabetic retinopathy (PDR) attending the retina clinic were included in this study. After detailed ocular examination and fundus fluorescein angiography, patients were treated with PRP. After PRP, visual acuity testing and retinal examination was done after 1 month, 3 months, 6 months and 1 year. Results: At baseline 30% eyes had visual

acuity of 6/6- 6/9, 44% had visual acuity of6/12-6/36 and 26% eyes had visual acuity of <6/60. 73.3% of patients with visual acuity 6/6- 6/9 at baseline retained their vision, 26.67% had decreased vision. 86.36% of patients with visual acuity 6/12- 6/36 at baseline retained their vision, 9.09% had decreased vision and 4.55% of patients had improved vision. 92.30% with poor baseline visual acuity (≤6/60) retained the same visual acuity and 7.69% of them improved to 6/9 at the end of 1 year. Causes of visual loss following PRPat the end of 1 year included vitreous hemorrhage (33.33%), pre retinal hemorrhage (33.33%), epiretinal membrane (33.33%), tractional retinal detachment (8.33%), macular edema (8%), choroidal effusion (8%), and acceleration of pre retinal fibrosis (8%). Conclusion:After PRP, visual acuity was maintained at baseline in majority of patients. However, decreased vision seen in few patients occured due to vitreous hemorrhage, pre retinal hemorrhage and macular edema.

(J Clin Biomed Sci 2011 ; 1 (3))

Relation between iridopathy and retinopathy in diabetes

Francesco Bandello, Rosario Brancato, Rosangela Lattanzio, Marcello Galdini, Bruno Falcomata

Abstract

In order to assess the relation between diabetic iridopathy (DI) and retinopathy (DR), 225 eyes of 117 diabetics with clear media were evaluated. Each patient underwent iris and retinal fluorescein angiography, which was used to classify DI and DR. DI was classified as: absence of DI; non-proliferative DI; proliferative DI; neovascular glaucoma. DR was classified as: absence of DR; background DR; pre-proliferative DR; proliferative DR. The sensitivity of iris fluorescein angiography in assessing DR was 44 5%, the specificity 88%, the positive predictive value 92i8%, and the negative value 31'2%. In pre-proliferative and proliferative DR, fluoroiridographic detection of iris neovessels gave a sensitivity of 56% and a specificity of 100%. The positive predictive value was 100% and the negative value 65%. In conclusion, iris fluorescein angiography yields valuable information on DR and is a helpful basis for avoiding complications when scheduling eyes with dioptric media opacities or surgery.

(BrJ7 Ophthalmol 1994; 78: 542-545)

PART II

AIMS AND OBJECTIVES

- To analyse the role of visual evoked potential in determining the amount of retinal nerve fibre loss in patients who underwent panretinal photocoagulation.
- To analyse the changes in visual evoked potential response and correlate with its visual prognosis.

STUDY PERIOD

- 8 months.

STUDY DESIGN

- A prospective,cross sectional study .

MATERIALS AND METHODS:

- Diabetic mellitus patients are to be recruited from inpatients and outpatients of ophthalmology department, GRH,Madurai.

SAMPLE SIZE:

- 50 patients

THE INCLUSION CRITERIA

- Type 2 diabetic patients with diabetic retinopathy who satisfied criteria for panretinal photocoagulation as recommended by EDTRS.

THE EXCLUSION CRITERIA

- Patients with media opacity like corneal opacity,vitreous heamorrhage,mature cataract which hamper posterior segment examination and VEP recording.
- Poor cooperative patient.
- Patients with poor fixation as in nystagmus, Amblyopia.
- One eyed patients.
- Previous laser treatment.
- Patients not giving consent for study.

FINANCIAL SUPPORT: Nil

METHODOLOGY

- Patients satisfying inclusion criteria are selected.
- Explain about the study and procedure and get informed consent.
- Initial Visual acuity is recorded by Snellen's chart.
- Anterior segment examination by torch light and slit lamp biomicroscopy.
- Pupillary examination (both direct, consensual and swinging flash light test) by pupilloscope.
- Colour vision tested by psuedoisochromatic ishihara's color vision chart
- Visual fields by Humphrey field analysis.
- Tension by Goldmann applanation tonometry
- Fundus examination by direct ophthalmoscope or by using +90D lens with slit lamp are recorded.
- Fundus color photo,red free photograph taken by fundus camera.
- VEP performed in sitting position before PRP .

- Panretinal photocoagulation done as per the indication over 2 to 3 session.
- Repeat the examination and VEP after 6 weeks
- Patients are asked to review after 6th month for follow up.

Discussion

Even though laser pan retinal photocoagulation is the mainstay of treatment for diabetic retinopathy,it is not devoid of adverse effect due to irresistible ganglion cell loss and nerve fibre layer damage. Diabetic mellitus itself cause both vasculopathy and neuropathy. retinal neurodegeneration is the primary manifestation of ocular diabetic changes.In this study,we analyse the changes in VEP in diabetic retinopathy patients before undergoing PRP and correlate it with visual outcome and prognosis after PRP.

OBSERVATION AND ANALYSIS

TABLE 1: AGE DISTRIBUTION OF THE STUDY POPULATION

Age in years	No.of cases
< 45	13
46 - 55	10
56 - 65	13
> 65	14
Total	50

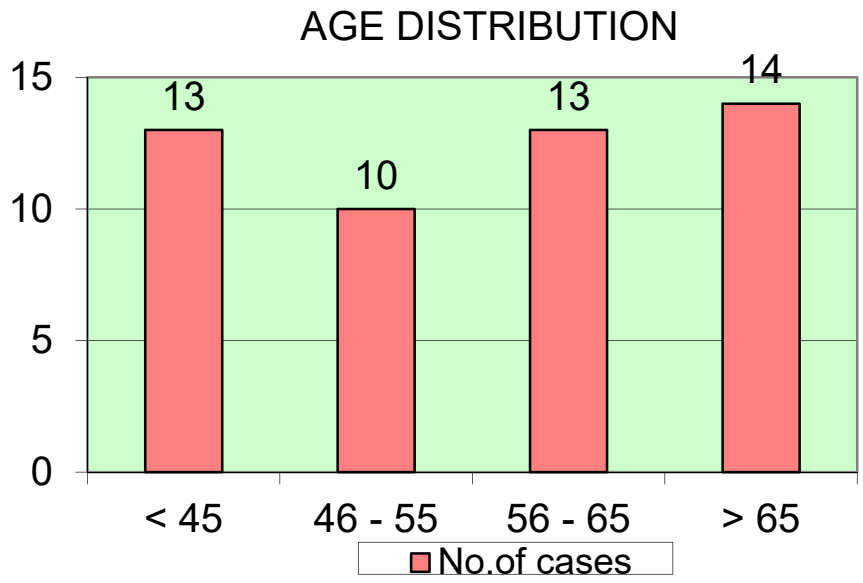


Table 1 and GRAPH show that in our study the age distribution of patients was within 38-75 years with majority falling between 50-55 years.

TABLE 2: DISTRIBUTION OF SEVERITY OF DIABETIC RETINOPATHY

Distribution of DR	No.of eyes
Grade 1	10
Grade 2	38
Grade 3	52

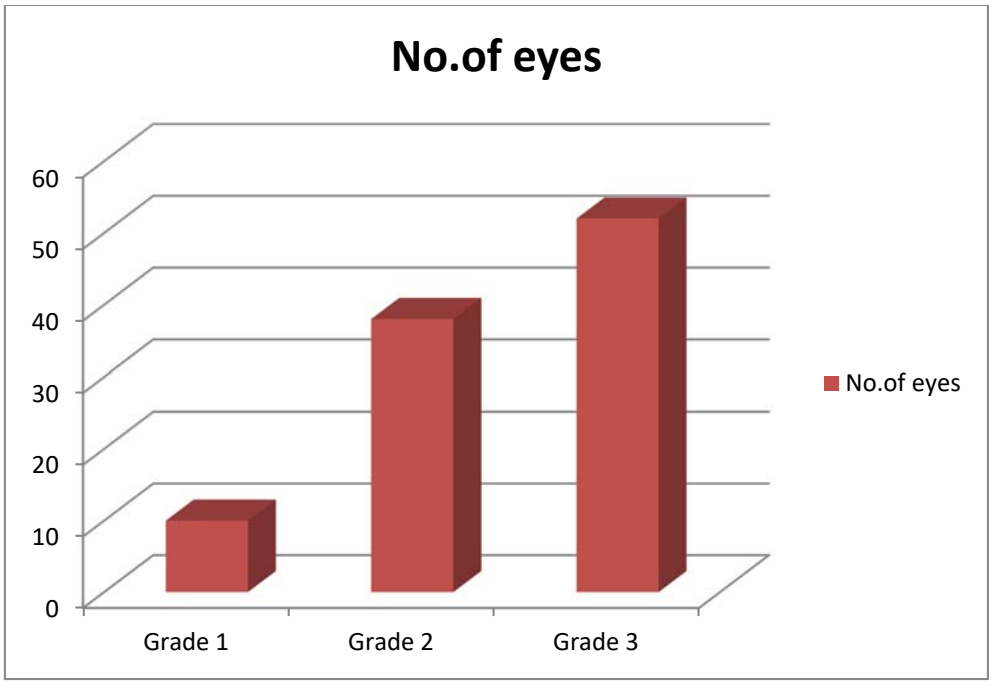


Table 2 shows distribution of diabetic retinopathy in our study.52% patient had grade 3 DR,38% had grade 2 DR,10% had grade 1.As expected ,PDR patients are more in this group who is going for PRP.

TABLE 3: MEAN VEP CHANGES WITH SEVERITY OF DR

Severity of DR	PrePRP VEP Mean
Grade 1 (10)	11.3
Grade 2 (38)	8.6
Grade 3 (52)	6.2
P VALUE	<0.001 Significant

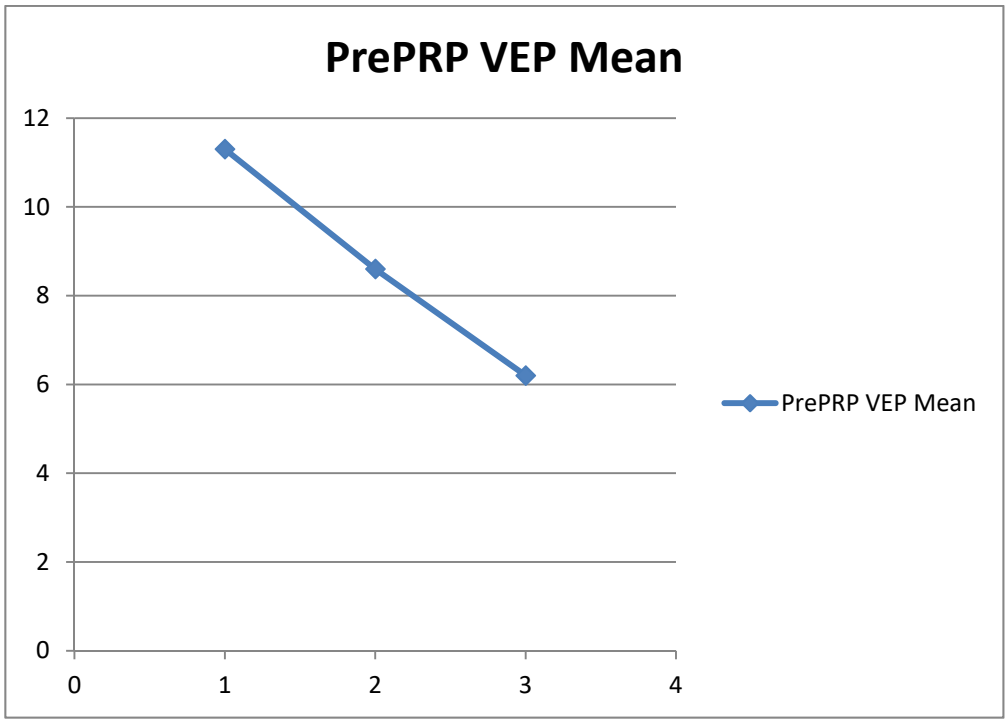
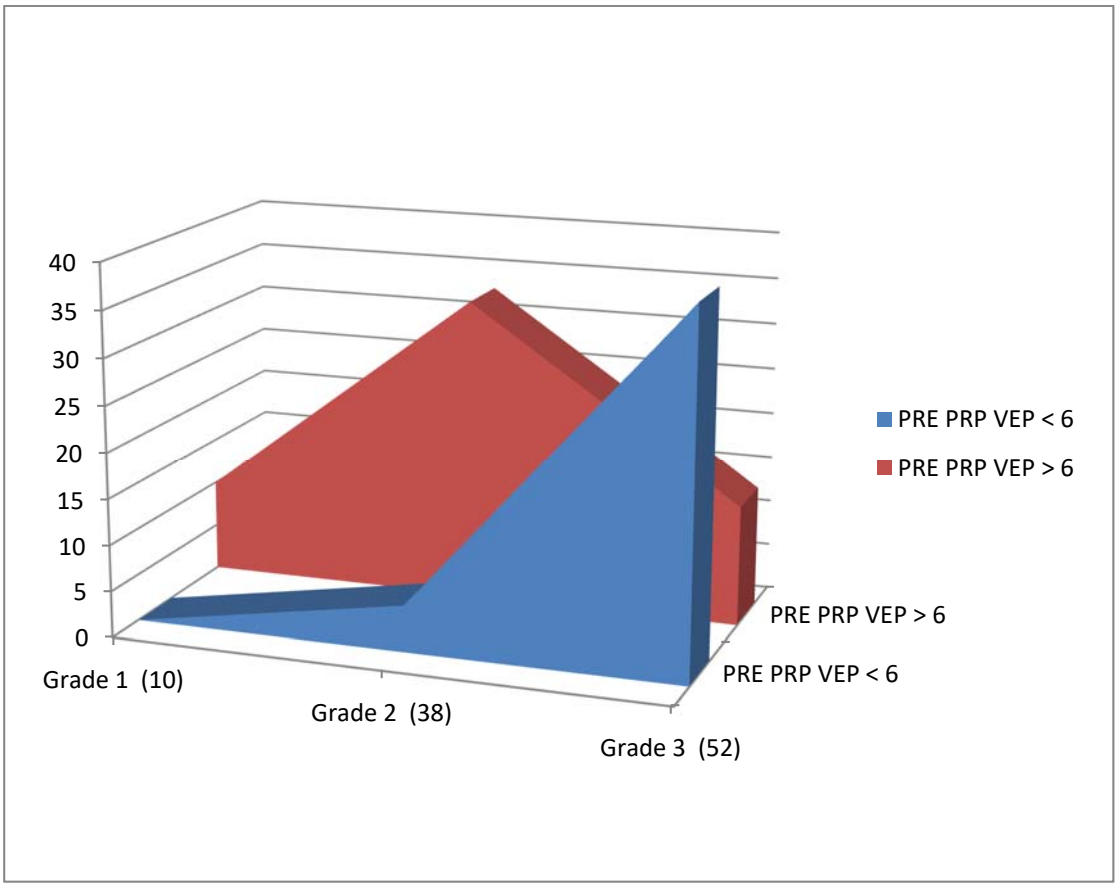


Table 3 shows mean VEP of grade3is 6.2 µv, grade 2 is 8.6 µv, grade 1 is 11.3 µv. Diabetic retinopathy severity increase with decreases in VEP amplitude.VEP amplitude shows directly correlated with severity of damage due to DR.

TABLE 4: PRE PRP VEP IN DR

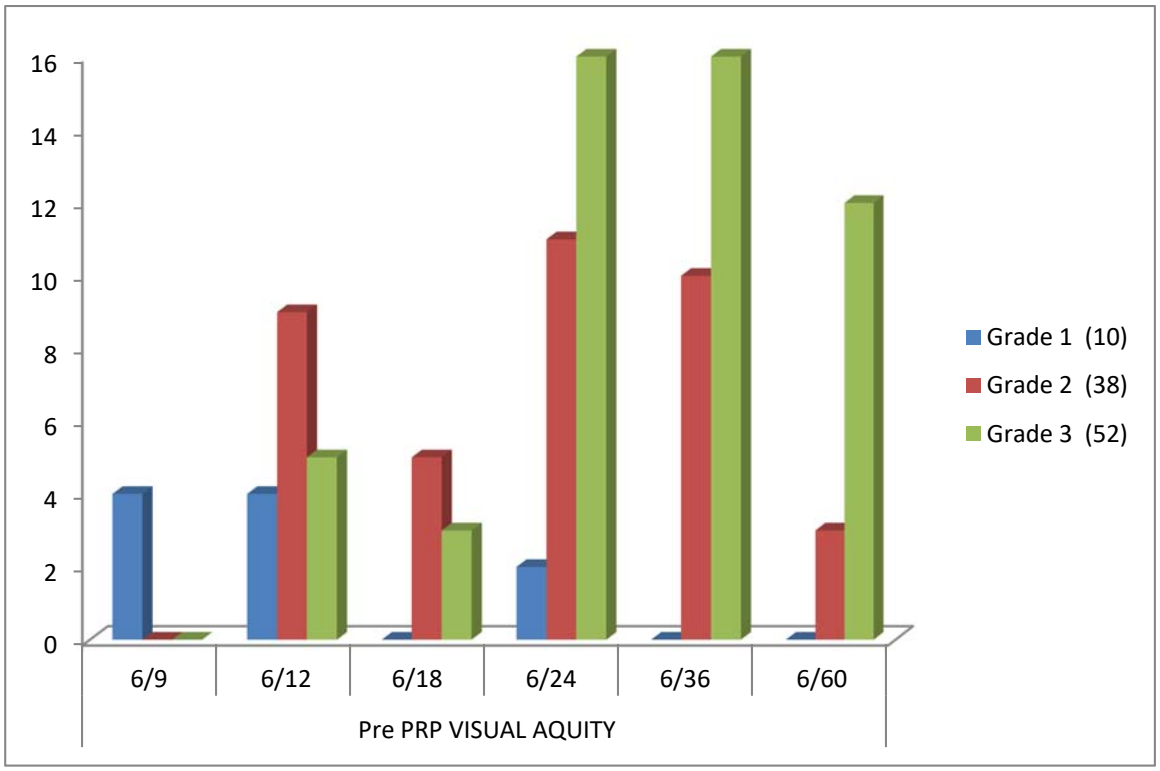
PRE PRP VEP amplitude µV		
DR	< 6	> 6
Grade 1 (10)	0	10
Grade 2 (38)	5	33
Grade 3 (52)	39	13



This table shows grade 1(100%) and grade 2 (86%) patients had VEP amplitude more than 6µV whereas grade 3 (75%) patients had VEP amplitude ≤ 6 µV.

TABLE 5: PRE PRP VA in DR

	Pre PRP VISUAL AQUITY					
	6/9	6/12	6/18	6/24	6/36	6/60
Grade 1 (10)	4	4	0	2	0	0
Grade 2 (38)	0	9	5	11	10	3
Grade 3 (52)	0	5	3	16	16	12



In study, 16 grade 3 patients had VA of 6/24 (27%) and and 6/36(27%) and 11 grade 2 patients had VA of 6/24(28%) and 4 grade 1 patients had 6/9 and 6/12(40%).

TABLE 6: POST PRP VA IN DR

	Post PRP VISUAL AQUITY									
	6/12	6/18	6/24	6/36	6/60	5/60	3/60	HM	PL+	PL-
Grade 1 (10)	1	2	2	2	1	0	0	0	0	0
Grade 2 (38)	0	1	8	11	12	3	0	1	1	1
Grade 3 (52)	0	0	4	7	21	10	2	3	3	0

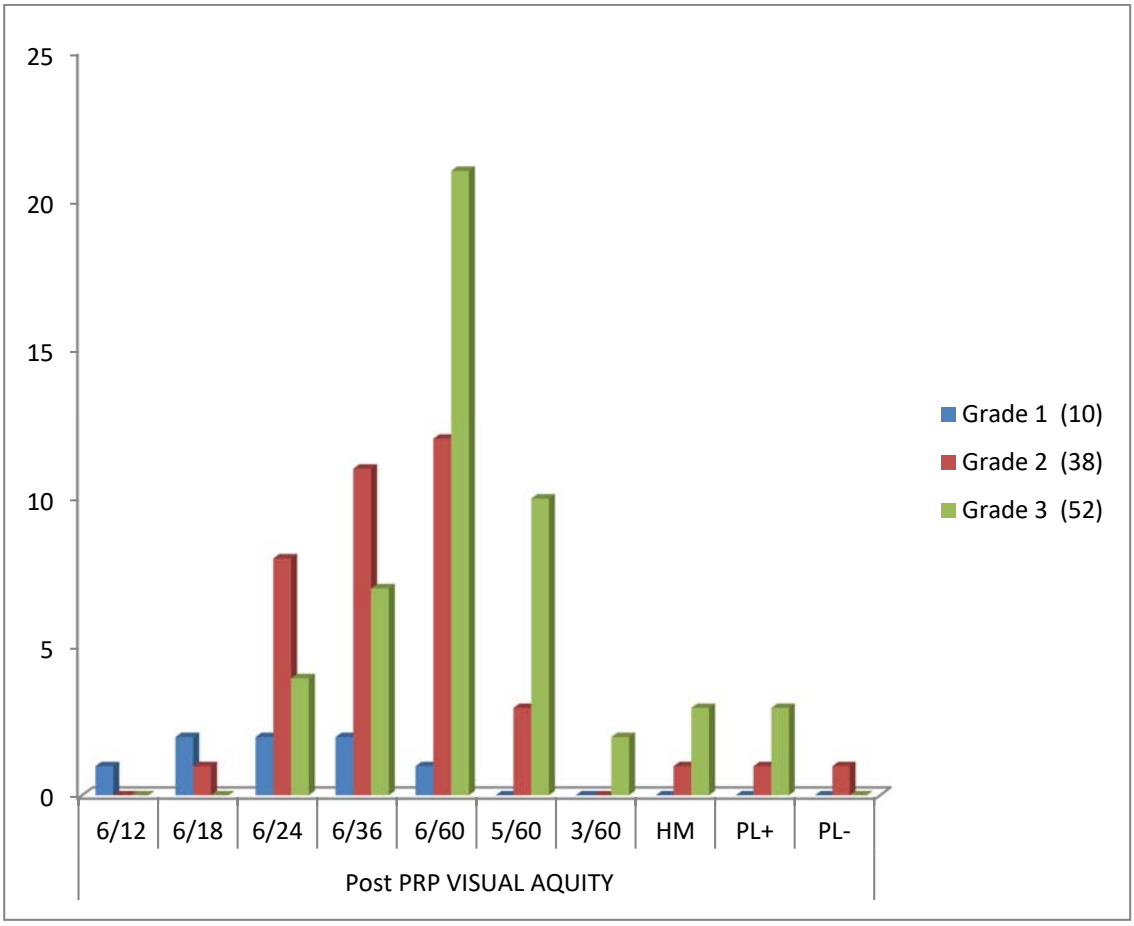
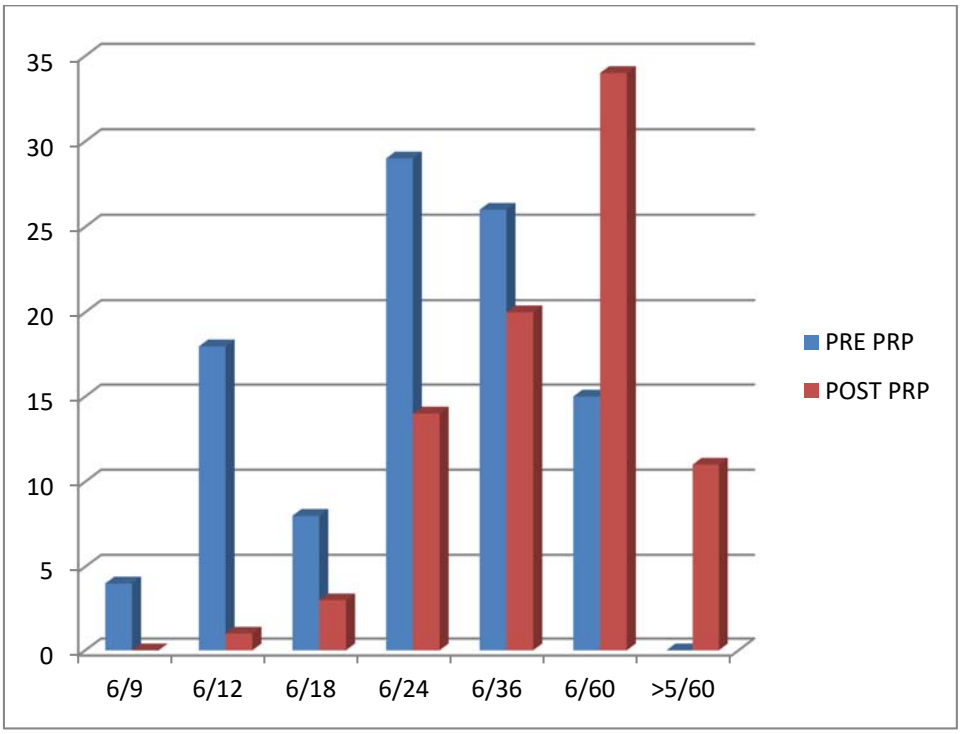


TABLE 7:PRE PRP VA VS POST PRP VA

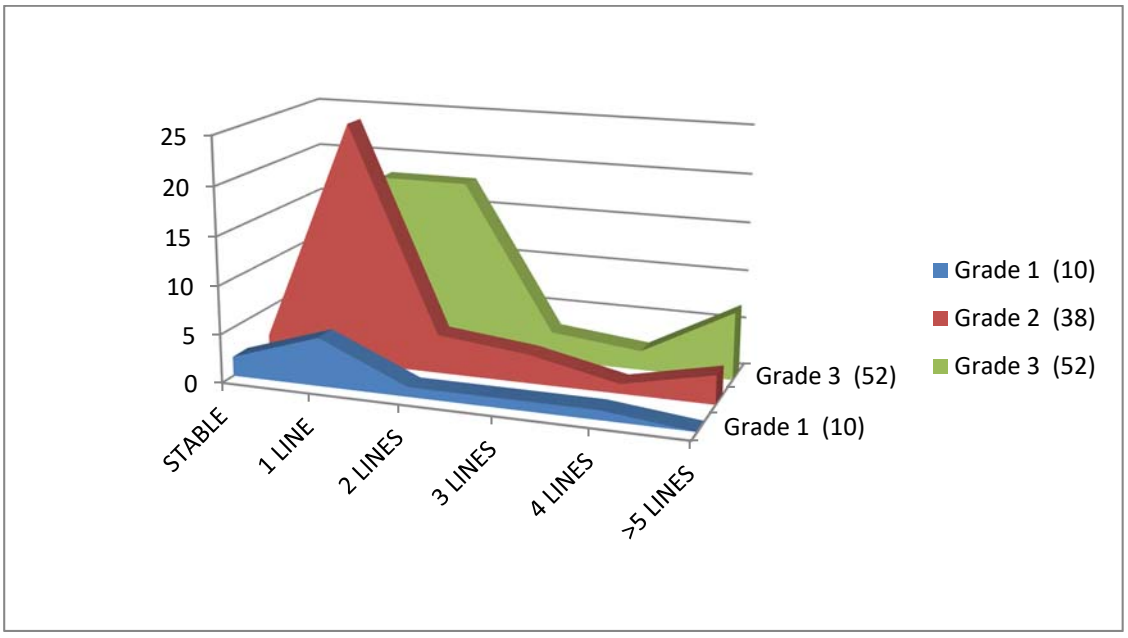
VA	PRE PRP	POST PRP
6/9	4	0
6/12	18	1
6/18	8	3
6/24	29	14
6/36	26	20
6/60	15	34
>5/60	0	11



Here,>5/60 VA seen only after PRP .34 post PRP patients had 6/60 where only 15 pre PRP patient had 6/60.From the above two table,there is detoriation of vision seen after PRP.

TABLE 8: CORRELATION OF VA DETORIATION AFTER PRP WITH SEVERITY OF DR

VA DETORIATION IN SNELLENS AFTER PRP						
DR	STABLE	1 LINE	2 LINES	3 LINES	4 LINES	>5 LINES
Grade 1 (10)	2	5	1	1	1	0
Grade 2 (38)	2	25	4	3	1	3
Grade 3 (52)	4	18	18	3	2	7



In this study,50% of grade 1 patient had detoriation of VA of 1 line in snellens and no one detoriated >5 lines.65% of grade 2 patients detoriated VA of 1 line and 3 patients had >5 lines drop.34% of grade 3 patients had 1 line drop in VA but 7 patients had >5 line drop.thus ,there is significant reduction in VA after PRP which is more with grade 3 DR.

TABLE 9: PRE PRP VEP AND POST PRP VEP

VEP AMPLITUDE μv	Pre PRP VEP	Post PRP VEP
> 6	56	36
< 6	44	64
Mean	7.6	5.3
SD	2.59	2.74
p value	< 0.001	Significant

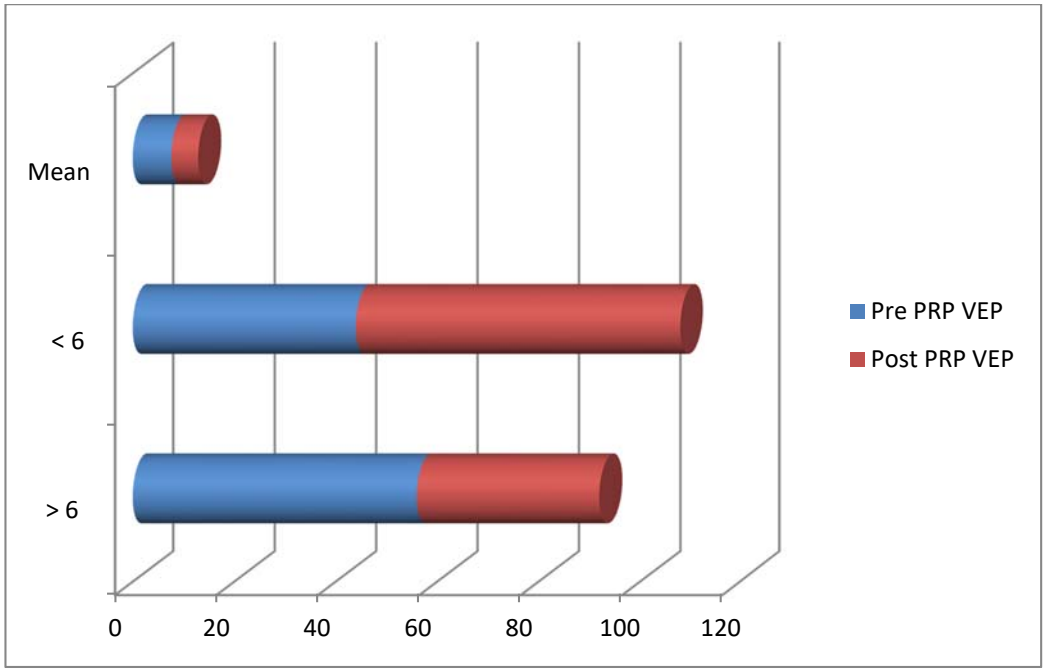
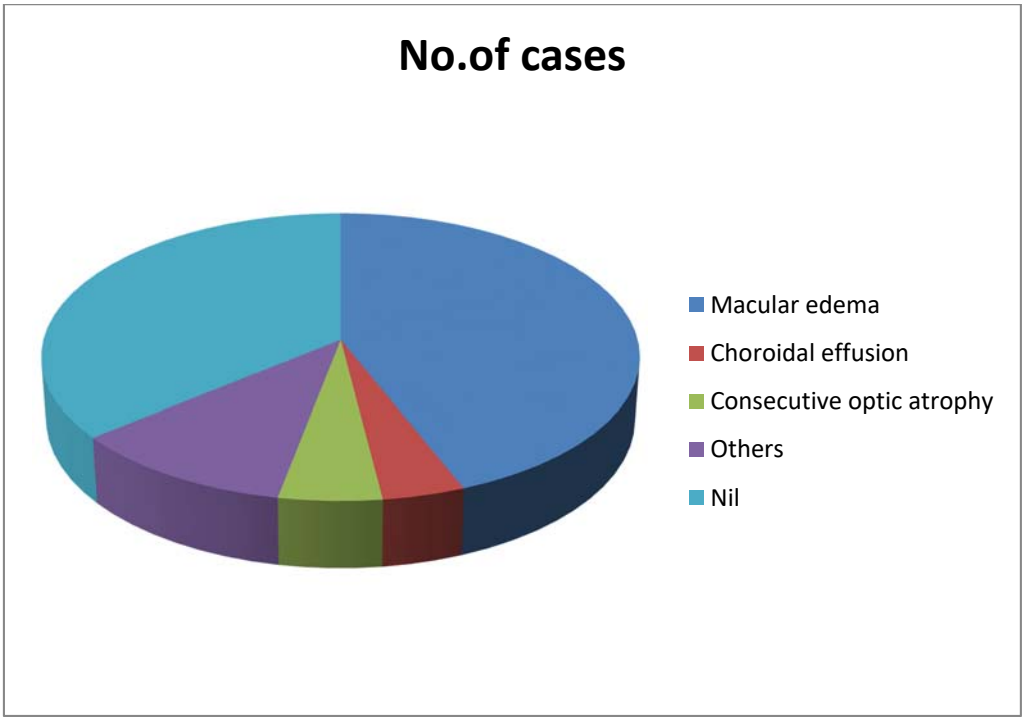


Table 8 shows mean value of pre PRP VEP is 7.72 and Post PRP VEP is 3.95.there is significant reduction in VEP after PRP.

TABLE 10: COMPLICATIONS AFTER PRP

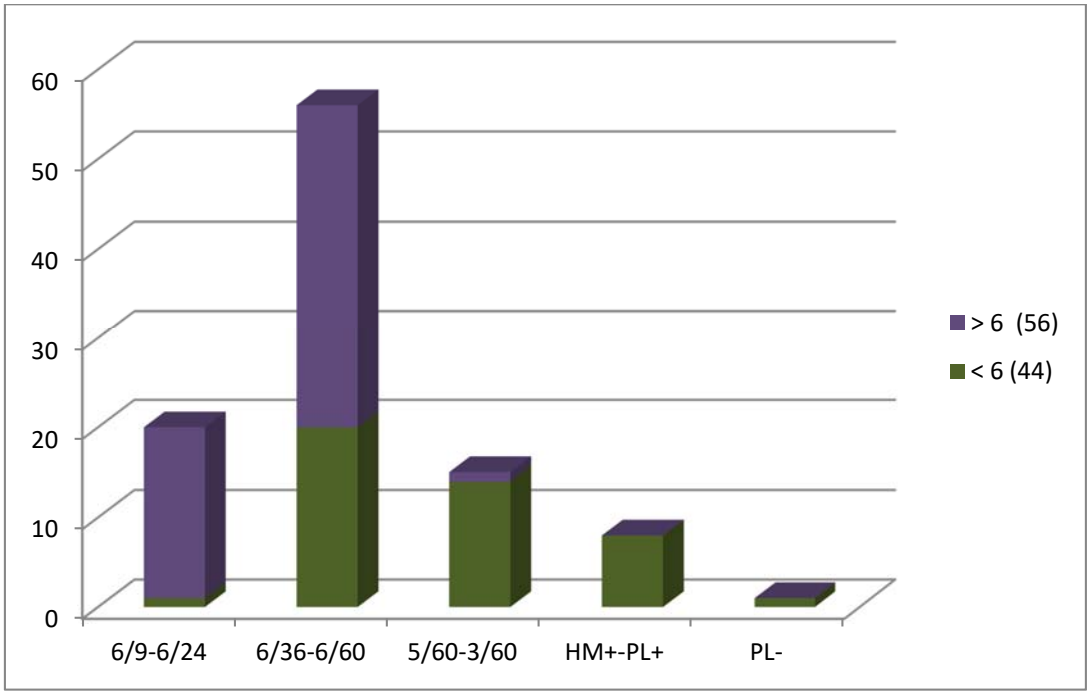
Complication	No.of cases
Macular edema	44
Choroidal effusion	4
Consecutive optic atrophy	5
Others	11
Nil	36



In our 44 % had macular edema and 36% had no complications.

TABLE 11: CORRELATION OF PRE PRP VEP WITH POST PRP VA

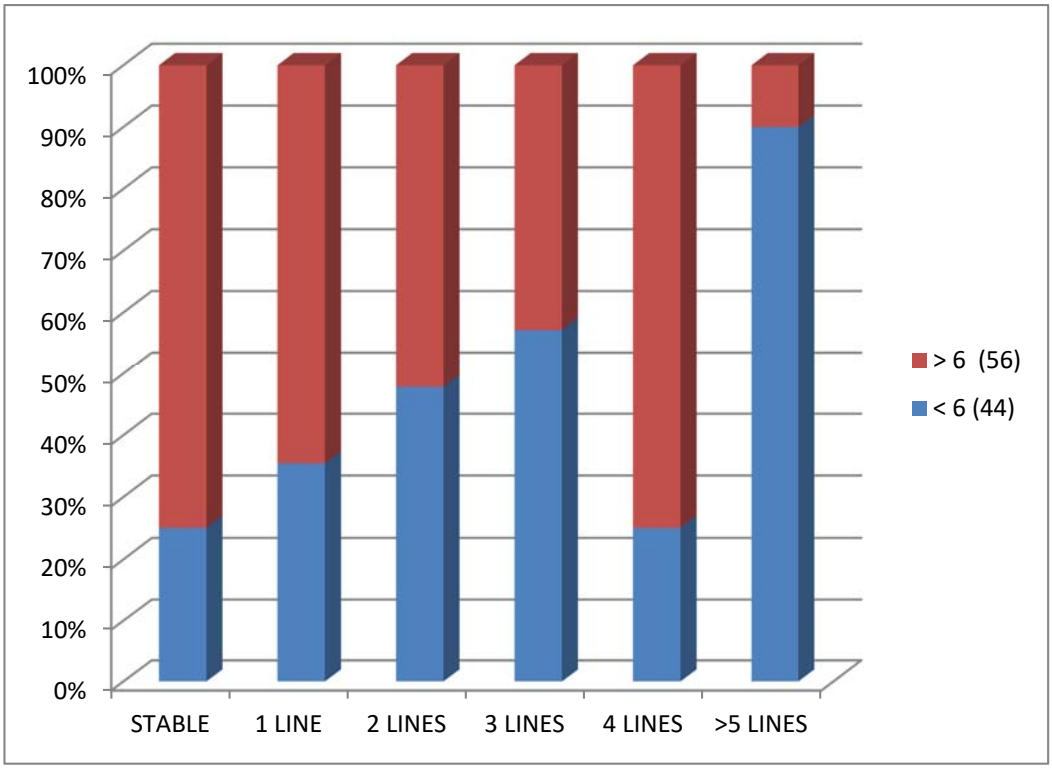
POST PRP VA					
PRE PRP VEP amplitude µV	6/9-6/24	6/36-6/60	5/60-3/60	HM+-PL+	PL-
< 6 (44)	1	20	14	8	1
> 6 (56)	19	36	1	0	0



In patients with Pre PRP VEP < 6 µV ,14 patients had 5/60 - 3/60(31%),8 patients had HM-PL+(18%),1 patient had PL-(2%).where in > 6 µV,1 had 5/60-3/60(1%),no patients had HM and less.so, when pre PRP VEP is < 6 µV ,there is detoriation of vision up to PL – as compared to amplitude > 6 µV.

TABLE 12: PRE PRP VEP Vs POST PRP VA

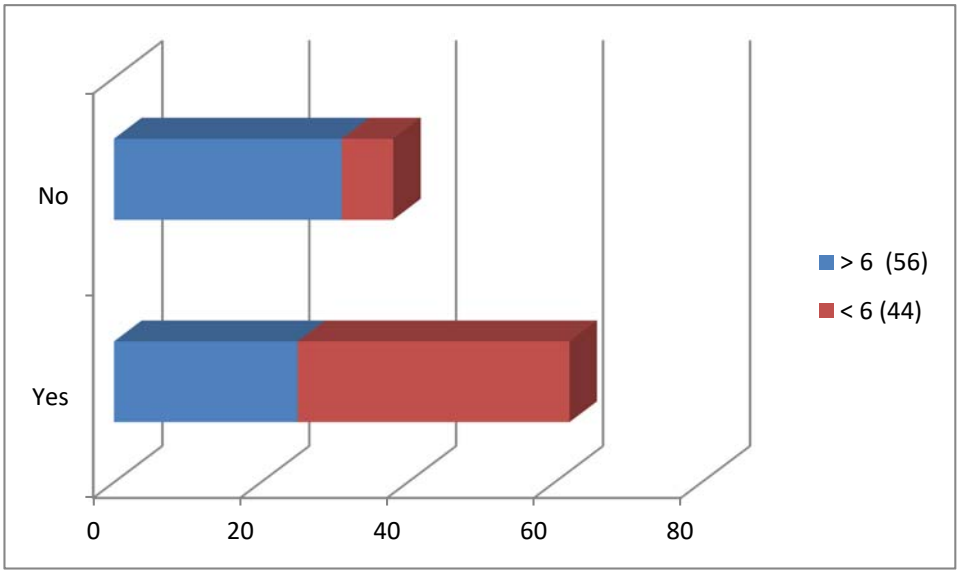
VA DETORIATION IN SNELLENS AFTER PRP						
PRE PRP VEP amp µV	STABLE	1 LINE	2 LINES	3 LINES	4 LINES	>5 LINES
< 6 (44)	2	17	11	4	1	9
> 6 (56)	6	31	12	3	3	1



From above 2 tables, when VEP < 6 µV,there is statistically significant reduction VA($p<0.001$).

TABLE 13: PRE PRP VEP Vs COMPLICATIONS

	Complications	
VEP	Yes	No
> 6 (56)	25	31
< 6 (44)	37	7
p value	0.001	Significant



In patients with Pre PRP VEP is < 6 µV, 37 had complication (84%), where >6 µV 25 had complications (44%).this statistical analysis shows complication is more when pre PRP VEP is< 6µV with p<0.001.

From above study, data was analysed with SPSS statistical software package (version 16.0 SPSS Inc Chicago,USA). The changes in VEP after PRP was analysed by using paired t test,$p<0.001$ will be considered as statistically significant. Complications associated with decreased VEP analysed by chi square test, $p<0.001$ considered as statistically significant.

DISCUSSION

Visual evoked potential is a measurement of electrical signal of occipital cortex in response to light stimulus. Abnormalities in VEP denote a nonselective functional neuronal loss .it reveals integrity of afferent visual pathway or any damage along the visual pathway. Therefore, VEP should be considered as a valid method for detecting neuronal damage (ganglion cell and nerve fibre layers of the retina)in diabetic retinopathy.

Diabetic mellitus can leads to visual impairment by both diabetic retinopathy and neurodegeration. In an compromised retina in DR, laser axotomy also leads to wallarian degeneration of retinal ganglion cells.

Though Pan retinal photocoagulation is considered to be a mainstay of treatment for PDR, its complication can also even worsen the vision such as macular edema, peripheral visual field loss, consecutive optic atrophy, choroidal effusion.

In our study, we try to analyse and establish the role of VEP in assessing preexisting retinal nerve damage due to diabetic retinopathy. Thus, VEP helps in predicting the retinal nerve status in patients with diabetes who is going for laser treatment. Early detection of complication and visual prognosis by VEP can change the mode of

treatment includes Intra vitreal anti-VEGFor adjust the parameter of laser burns like PASCAL,MIP.

In our study, we had taken one hundred eyes of fifty patients with diabetic retinopthy who is fit for pan retinal photocoagualation according to EDTRS classification.

In this study, age of the patients distribution ranges around 50-55 years of age.Mean Pre PRP VEP amplitude is significantly decreases with severity of diabetic retinopathy($P<0.001$).it shows strong correlation with severity of DR and abnormal VEP which may attributed for extensive retinal nerve damage in grade 3 diabetic retinopathy.

Mean pre PRP VEP amplitude is 7.6μV and post PRP VEP amplitude is 5.3μV.A statistically significant number of patients shows reduced VEP after PRP.

In this study, macular edema is more frequently seen (44%) followed by nil complication(36%), choroidal effusion (4%),COA(5%), other(11%). Complications followed by laser is equally distributed among 3 grades of DR.

When Pre PRP VEP amplitude is $\leq$ 6μV, there is significant reduction in post PRP VA and complications.As diabetic retinopathy and neuropathy leads to functional detoriation by significant thinning of the

ganglion cell and nerve fibre layer, complicatios of PRP is increase in already compromised retina.

CONCLUSION

From this study, we conclude that VEP can play a major role in assessing functional neuronal loss in DR. In severe NPDR, very severe NPDR and early PDR, consider full scatter Pan Retinal photocoagulation as an optional after doing VEP.when VEP amplitude is ≤6µV, we can modify the LAER parameter like spot size, energy, distance between spots or other newer modalities like selective retinal therapy (SRT)transpupillary thermotherapy (TTT) ,subvisible diode micropulse (SDM) photocoagulation and other treatment like intra vitreal anti-VEGF.

LIMILATIONS

- In this study, only 5 grade 2 DR patient had VEP amplitude ≤ 6µV.
- We are not discussed about inadequate PRP that may lead to neovascularization after subthreshold PRP.
- Small sample size

ANNEXURES

ANNEXURES

ANNEXURE I -BIBLIOGRAPHY

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ANNEXURE II-ABBREVIATIONS USED IN THIS STUDY

VEP - VISUAL EVOKED POTENTIAL

DR - DIABETIC RETINOPATHY

DD - DISC DIAMETER/DISC DIOPTER

NVG - NEOVASCULAR GLAUCOMA

FFA - FUNDUS FLUORESCEIN ANGIOGRAPHY

MA - MICRO ANEURYSMS

BDR - BACKGROUND DIABETIC RETINOPATHY

NVD - NEOVASCULARISATION OF DISC

NVE - NEOVASCULARISATION ELSEWHERE

CSME - CLINICALLY SIGNIFICANT MACULAR EDEMA

IRMA - INTRA RETINAL MICROVASCULAR ANOMALIES

NPDR - NON PROLIFERATIVE DIABETIC RETINOPATHY

PDR - PROLIFERATIVE DIABETIC RETINOPATHY

PRP - PAN RETINAL PHOTOCOAGULATION

VEGF - VASCULAR ENDOTHELIAL GROWTH FACTOR

PEDF - PIGMENT EPITHELIUM DERIVED FACTOR

ETDRS - EARLY TREATMENT OF DIABETIC RETINOPATHY STUDY

PRH - PRE RETINAL HEMORRHAGE

VH - VITREOUS HEMORRHAGE

RPE - RETINAL PIGMENT EPITHELIUM

µ - MICRON

nm - NANOMETRE

mm - MILLIMETRE

cm - CENTIMETRE

VA - VISUAL AQUITY

BRB - BLOOD RETINAL BARRIER

ANNEXURE III-MASTER CHART

S.No.	NAME	AGE	DIABETIC RETINOPATHY	PRE PRP VEP	Pre PRP Visual Acquity	POST PRP VEP	POST PRP VA	COMPLICATIONS
1	FATHIMA BEEVI	42	2	11	6/12	7	6/36	MACULAR EDEMA
2	FATHIMA BEEVI		2	11	6/24	8	6/36	NIL
3	CHELLADURAI	45	3	7	6/12	3	6/24	VISUAL FIELDS DEFECT
4	CHELLADURAI		1	11	6/12	4	6/60	MACULAR EDEMA
5	JAYALAKSHMI	50	2	11	6/12	9	6/24	VISUAL FIELDS DEFECT
6	JAYALAKSHMI		2	11	6/24	8	6/36	VISUAL FIELDS DEFECT
7	IBRAHIM	41	2	10	6/36	7	6/60	VISUAL FIELDS DEFECT
8	IBRAHIM		2	10	6/24	8	6/36	NIL
9	THIRUMOORTHI	39	1	13	6/12	11	6/18	NIL
10	THIRUMOORTHI		3	11	6/12	8	6/36	MACULAR EDEMA
11	SAVARIMUTHU	62	1	10	6/12	8	6/24	NIL
12	SAVARIMUTHU		3	4	6/60	1.2	PL+	COA
13	BASKAR	66	2	6	6/24	1.5	5/60	NV
14	BASKAR		3	6	6/24	3	6/60	MACULAR EDEMA
15	SURENDAR	72	3	6	6/24	4	6/60	MACULAR EDEMA
16	SURENDAR		3	7	6/36	5	6/60	NIL
17	ARJUNAN	69	3	6	6/12	4	6/24	NIL
18	ARJUNAN		3	6.5	6/12	1.6	3/60	MACULAR EDEMA
19	SOUNDARA PANDI	57	3	9	6/36	7	6/60	NIL
20	SOUNDARA PANDI		1	9	6/12	7	6/36	MACULAR EDEMA
21	AYYAPAN	59	2	10	6/36	8	6/60	VISUAL FIELDS DEFECT
22	AYYAPAN		2	10	6/36	7	6/60	VISUAL FIELDS DEFECT

23	IRULLAPPAN	61	3	5	6/60	3.5	6/60	NIL
24	IRULLAPPAN		1	10	6/9	9	6/18	NIL
25	SATHAIYA	40	3	10	6/24	5	6/60	MACULAR EDEMA
26	SATHAIYA		1	12	6/9	10	6/12	NIL
27	SUBRAMANIYAN	38	3	9	6/12	6	6/24	VISUAL FIELDS DEFECT
28	SUBRAMANIYAN		2	9	6/36	6	6/60	VISUAL FIELDS DEFECT
29	PANDIYAMMAL	42	2	11	6/12	9	6/24	NIL
30	PANDIYAMMAL		2	11	6/36	9	6/60	VISUAL FIELDS DEFECT
31	SHENBAGARAJ	68	3	6	6/60	3.5	5/60	NIL
32	SHENBAGARAJ		3	4	6/24	0.8	PL+	COA
33	JAYAKUMAR	67	2	4	6/60	1	PL-	COA
34	JAYAKUMAR		2	8	6/18	6	6/24	NIL
35	MAYANDI	69	3	6.5	6/18	3	6/36	MACULAR EDEMA
36	MAYANDI		3	3	6/60	2	PL+	COA
37	MUTHUKUMAR	57	2	7	6/12	5	6/36	MACULAR EDEMA
38	MUTHUKUMAR		2	5	6/24	2	PL+	COA
39	PALANIVEL	64	3	6	6/36	4	6/36	NIL
40	PALANIVEL		3	6	6/36	3	6/60	VISUAL FIELDS DEFECT
41	SUNDARI	60	3	6	6/24	4	6/36	NIL
42	SUNDARI		3	6	6/36	3.5	6/60	NIL
43	PAL WILLIAM	55	2	8	6/18	5	6/36	MACULAR EDEMA
44	PAL WILLIAM		2	8	6/36	6	6/60	NIL
45	PETCHIYAMMAL	65	3	5	6/18	3.2	6/60	MACULAR EDEMA
46	PETCHIYAMMAL		3	5	6/24	2	5/60	MACULAR EDEMA
47	JOSEPH RAJA	49	2	8	6/18	7	6/24	NIL
48	JOSEPH RAJA		2	5	6/12	1.6	HM	CHOROIDAL EFFUSION
49	BALASUBRAMANIYAM	43	2	9	6/36	7	6/60	VISUAL FIELDS DEFECT

50	BALASUBRAMANIYAM		2	9	6/24	6	6/36	VISUAL FIELDS DEFECT
51	PALANIMUTHAMAL	46	2	8	6/24	6	6/36	NIL
52	PALANIMUTHAMAL		2	8	6/12	7	6/24	MACULAR EDEMA
53	INDRAGANDHI	38	1	12	6/24	10	6/24	NIL
54	INDRAGANDHI		3	12	6/24	9	6/36	VISUAL FIELDS DEFECT
55	MURUGAN	70	3	4	6/36	1.5	HM	CHOROIDAL EFFUSION
56	MURUGAN		3	4	6/60	1	HM	CHOROIDAL EFFUSION
57	JAILANI	67	3	5	6/36	1.2	3/60	MACULAR EDEMA
58	JAILANI		3	5	6/24	3	6/60	MACULAR EDEMA
59	JOTHI	68	3	7	6/60	4	6/60	NIL
60	JOTHI		3	6	6/24	4	6/60	MACULAR EDEMA
61	SATHYAMOORTHI	46	2	11	6/36	12	6/36	NIL
62	SATHYAMOORTHI		2	9	6/24	7	6/36	VISUAL FIELDS DEFECT
63	POOMIRAJA	49	3	6	6/60	3	5/60	NIL
64	POOMIRAJA		3	6	6/36	5	6/60	VISUAL FIELDS DEFECT
65	ALAGAMMAL	56	2	10	6/36	7	6/60	NIL
66	ALAGAMMAL		2	10	6/12	8	6/24	NIL
67	PALPANDI	59	2	9	6/36	8	6/60	VISUAL FIELDS DEFECT
68	PALPANDI		2	9	6/24	7	6/36	NIL
69	MEENATCHIAMMAL	63	3	6	6/36	5	6/60	NIL
70	MEENATCHIAMMAL		3	6	6/60	4	5/60	VISUAL FIELDS DEFECT
71	SUBRAMANI	43	2	5	6/60	4	5/60	MACULAR EDEMA
72	SUBRAMANI		2	8	6/18	6	6/24	NIL
73	PANDI	67	3	6	6/36	3.4	6/60	MACULAR EDEMA
74	PANDI		3	6	6/24	5	6/60	MACULAR EDEMA
75	MURUGESAN	49	2	10	6/12	9	6/18	NIL
76	MURUGESAN		2	10	6/18	8	6/24	NIL

77	PANDIYAN	50	3	7	6/60	5	6/60	VISUAL FIELDS DEFECT
78	PANDIYAN		3	6	6/24	4.7	6/36	NIL
79	RAVICHANDRAN	65	3	6	6/36	3	5/60	MACULAR EDEMA
80	RAVICHANDRAN		3	6	6/36	4	5/60	MACULAR EDEMA
81	ANDIDEVAR	66	3	6.5	6/60	4	6/60	VISUAL FIELDS DEFECT
82	ANDIDEVAR		1	11	6/24	10	6/36	NIL
83	JAITHUN BEEVI	39	1	13	6/9	12	6/9	NIL
84	JAITHUN BEEVI		3	13	6/24	10	6/36	NIL
85	ABDUL RAHMAN	45	3	4	6/24	2.8	5/60	MACULAR EDEMA
86	ABDUL RAHMAN		3	4	6/36	2.5	5/60	MACULAR EDEMA
87	THIRUMANI	38	1	12	6/9	10	6/12	NIL
88	THIRUMANI		3	12	6/18	10	6/24	NIL
89	RAJKUMAR	69	3	4	6/24	2	5/60	MACULAR EDEMA
90	RAJKUMAR		3	4	6/60	2	HM	CHOROIDAL EFFUSION
91	KASTHURI	62	3	5	6/24	4	6/60	VISUAL FIELDS DEFECT
92	KASTHURI		3	5	6/36	3	6/60	VISUAL FIELDS DEFECT
93	PANDIYAMMAL	66	3	5	6/24	3	6/60	MACULAR EDEMA
94	PANDIYAMMAL		3	5	6/60	4	5/60	VISUAL FIELDS DEFECT
95	DEVAGI	54	2	9	6/60	7	6/60	VISUAL FIELDS DEFECT
96	DEVAGI		2	5	6/24	4	5/60	MACULAR EDEMA
97	MALLIGA	67	3	6	6/36	4	6/60	VISUAL FIELDS DEFECT
98	MALLIGA		3	6	6/36	5	6/60	VISUAL FIELDS DEFECT
99	RAMAN	51	2	7	6/12	5	6/60	MACULAR EDEMA
100	RAMAN		2	8	6/24	6	6/60	VISUAL FIELDS DEFECT

ANNEXURE IV- PROFORMA

NAME: **AGE:** **SEX:**

ADDRESS: **PHONE NUMBER:** **OP/IP NO:**

CHIEF COMPLIANT:

H/O PRESENT ILLNESS:

PREVIOUS OCULAR SURGERY: CATARACT /TRABECULECTOMY

H/O ANTIGLAUCOMA MEDICATION: YES/NO

SYSTEMIC ILLNESS: HYPERTENSION/HYPOTHYROID/SEIZURE DISORDER/NEURODEGENERATIVE DISORDER/INFLAMMATORY DISEASE

STAGES OF DR: SEVERE NPDR /EARLY PDR /HIGH RISK PDR

WITH MACULOPATHY: YES/NO

ASSOCIATED WITH REFRACTIVE ERROR:

MYOPE/HYPEROPE/ASTIGMATISM/PRESBYOPE/NIL

OCULAR EXAMINATION:

BEFORE PRP

RE	PARAMETERS	LE
	UNCORRECTED VISUAL ACUITY	
	BEST CORRECTED VISUAL ACUITY	
	ANTERIOR SEGMENT	
	INTRA OCULAR PRESSURE	
	VISUAL FIELD	
	COLOUR VISION	
	GONIO	
	DIALATED FUNDUS	
	VEP -AMPLITUDE	
	VEP-LATENCY	
	FBS	
	PPBS	
	HbA1C	

AFTER 6 WEEKS OF PRP

RE	PARAMETERS	LE
	UNCORRECTED VISUAL ACUITY	
	BEST CORRECTED VISUAL ACUITY	
	ANTERIOR SEGMENT	
	INTRA OCULAR PRESSURE	
	VISUAL FIELD	
	COLOUR VISION	
	GONIO	
	DIALATED FUNDUS	
	VEP -AMPLITUDE	
	VEP-LATENCY	
	FBS	
	PPBS	
	HbA1C	

AFTER 6th MONTH OF PRP

RE	PARAMETERS	LE
	UNCORRECTED VISUAL ACUITY	
	BEST CORRECTED VISUAL ACUITY	
	ANTERIOR SEGMENT	
	INTRA OCULAR PRESSURE	
	VISUAL FIELD	
	COLOUR VISION	
	GONIO	
	DIALATED FUNDUS	
	FBS	
	PPBS	
	HbA1C	

ANNEXURE V- CONSENT FORM IN REGIONAL LANGUAGE

(TAMIL)

ஆராய்ச்சி ஒப்புதல் படிவம்

தேதி:

ஆராய்ச்சி தலைப்பு

பெயர்:

வயது: உள்நோயாளி எண்:

பால்: ஆராய்ச்சி சேர்க்கை எண்:

இந்த ஆராய்ச்சியின் விபரங்களும் அதன் நோக்கங்களும் முழுமையாக எனக்கு விளக்கப்பட்டது. எனக்கு விளக்கப்பட்ட விஷயங்களை புரிந்துகொண்டு எனது சம்மதத்தை தெரிவிக்கிறேன்.

இந்த ஆராய்ச்சியில் பிறரின் நிர்பந்தமின்றி என் சொந்த விருப்பத்தின் பேரில் நான் பங்கு பெறுகிறேன், மற்றும் நான் இந்த ஆராய்ச்சியிலிருந்து எந்த நேரமும் பின்வாங்கலாம் என்பதையும், அதனால் எந்த பாதிப்பும் ஏற்படாது என்பதையும், நான் புரிந்து கொண்டேன்.

நான் என்னுடைய சுயநினைவுடன் மற்றும் முழு சுதந்திரத்துடன் இந்த மருத்துவ ஆராய்ச்சியில் என்னை சேர்த்துக்கொள்ள சம்மதிக்கிறேன் முடிவுகளை அல்லது கருத்துக்களை வெளியிடும் போதோ அல்லது ஆராய்ச்சியின் போதோ என்னுடைய பெயரையோ அல்லது அடையாளங்களையோ வெளியிடமாட்டார்கள் என்பதையும் அறிந்து கொண்டேன்.

எனது நோயின் தன்மை மற்றும் பின்விளைவுகளையும் முழுமையாக புரிந்துகொண்டேன். இந்த ஆராய்ச்சியில் எனது நோயின் மூலக்கூறு மற்றும் தன்மையை மட்டுமே ஆராய்வார்கள் என்பதை அறிந்து கொண்டேன்.

இதனால் என் வைத்திய முறைகளில் எந்த மாற்றமும் பார்வைத்திறனில் எந்தவித பாதிப்பும் ஏற்படாது என்பதையும் தெரிந்துகொண்டேன். எனக்கு விளக்கப்பட்ட விஷயங்களை முழுமையாக புரிந்துகொண்டு இந்த ஆராய்ச்சியில் பங்குகொள்ள என் முழு மனதுடன் ஒப்புக்கொள்கிறேன்.

ஆராய்ச்சியாளர் கையொப்பம் பங்கேற்பாளர் கையொப்பம்

தேதி:

ANNEXURE VI - RECEIPT FOR PLAGIARISM

Gmail jdheeba 13 <jdheeba13@gmail.com>

[Urkund] 7% similarity - jdheeba13@gmail.com

report@analysis.urkund.com <report@analysis.urkund.com> 9 October 2018 at 22:03
To: jdheeba13@gmail.com

Document sent by: jdheeba13@gmail.com
Document received: 10/9/2018 6:32:00 PM
Report generated 10/9/2018 6:33:37 PM by Urkund's system for automatic control.

Student message:

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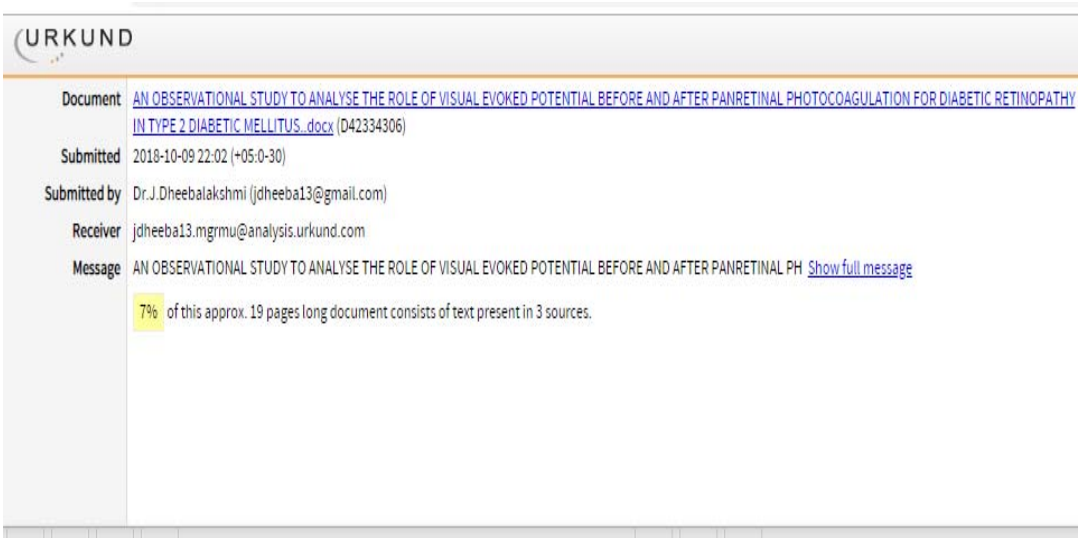
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Submitted	2018-10-09 22:02 (+05:0-30)
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ANNEXURE VII- ETHICAL CLEARANCE CERTIFICATE

MADURAI MEDICAL COLLEGE
MADURAI, TAMILNADU, INDIA -625 020
(Affiliated to The Tamilnadu Dr.MGR Medical University, Chennai, Tamil Nadu)

Prof Dr V Nagaraajan MD MNAMS DM (Neuro) DSc.,(Neurosciences) DSc (Hons)
Professor Emeritus in Neurosciences, Tamil Nadu Govt Dr MGR Medical University
Chairman, IEC

Dr.M.Shanthi, MD.,
Member Secretary,
Professor of Pharmacology,
Madurai Medical College, Madurai.

Members

1. Dr.V.Dhanalakshmi, MD, Professor of Microbiology & Vice Principal, Madurai Medical College

2. Dr.Sheela Mallika rani, M.D., Anaesthesia , Medical Superintendent Govt. Rajaji Hosptial, Maudrai

3.Dr.V.T.Premkumar,MD(General Medicine) Professor & HOD of Medicine, Madurai Medical & Govt. Rajaji Hospital, College, Madurai.

4.Dr.S.R.Dhamotharan, MS., Professor & H.O.D i/c, Surgery, Madurai Medical College & Govt. Rajaji Hosptial, Madurai.

5.Dr.G.Meenakumari, MD., Professor of Pathology, Madurai Medical College, Madurai

6.Mrs.Mercy Immaculate Rubalatha, M.A., B.Ed., Social worker, Gandhi Nagar, Madurai

7.Thiru.Pala.Ramasamy, B.A.,B.L., Advocate, Palam Station Road, Sellur.

8.Thiru.P.K.M.Chelliah, B.A., Businessman,21, Jawahar Street, Gandhi Nagar, Madurai.

ETHICS COMMITTEE CERTIFICATE

Name of the Candidate	:	Dr.J.Dheebalakshmi
Course	:	PG in MS., Ophthalmology
Period of Study	:	2016-2019
College	:	MADURAI MEDICAL COLLEGE
Research Topic	:	An observational study to Analysis the role of visual evoked potential before and after panretinal photocoagulation for diabetic retinopathy in type 2 diabetic mellitus.
Ethical Committee as on	:	16.05.2018

The Ethics Committee, Madurai Medical College has decided to inform that your Research proposal is accepted.

Member Secretary Chairman Dean / Convenor

Prof Dr V Nagaraajan
M.D., MNAMS, D.M., Dsc.,(Neuro), Dsc (Hon)
CHAIRMAN
IEC - Madurai Medical College
Madurai

DEAN
Madurai Medical College
Madurai-20

12 JUN 2018