

**COMPARATIVE STUDY BETWEEN PANRETINAL
PHOTOCOAGULATION VERSUS COMBINED PANRETINAL
PHOTOCOAGULATION AND INTRAVITREAL BEVACIZUMAB
INJECTION IN TREATMENT OF PROLIFERATIVE DIABETIC
RETINOPATHY**

Thesis

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List of Abbreviations

ANOVA: analysis of variance.

Anti-VEGF: anti-vascular endothelial growth factor.

AMD: age related macular degeneration.

BCVA: best corrected visual acuity.

DME: diabetic macular edema.

DR: diabetic retinopathy.

DRS: diabetic retinopathy study.

ELM: external limiting membrane.

ETDRS: early treatment of diabetic retinopathy study.

FAZ: foveal avascular zone.

FFA: fundus fluorescein angiography.

GCL: ganglion cell layer.

ICAM: intercellular adhesion molecule.

IOP: intraocular pressure.

ILM: internal limiting membrane.

INL: inner nuclear layer.

IPL: Inner plexiform layer.

IRMA: intra-retinal micro-angiopathy.

IVB: intravitreal bevacizumab injection.

IVR: intravitreal ranizumab injection.

Log. MAR: logarithm of minimal angle of resolution.

msec: milli- second.

mm²: milli-meter square.

NFL: nerve fiber layer.

nm: nanometer

NPDR:non proliferative diabetic retinopathy.

NV: neovascularization.

NVD: neovascularization at the disc.

OCT: optical coherence tomography.

ONL:outer nuclear layer.

OPL: outer plexiform layer.

PDR: proliferative diabetic retinopathy.

PKC:protein kinase C

PRP: pan-retinalphotocoagulation.

PPV: pars plana vitrectomy.

RPE: retinal pigmented epithelium.

SPSS: Statistical package for social sciences.

TRD: tractional retinal detachment.

um: micro meter.

VA: visual acuity.

VEGF: vascular endothelial growth factor

PROTOCOL

Protocol of thesis

Diabetic retinopathy is the most common microvascular complication of diabetes and remains one of the leading causes of blindness worldwide among adults aged 20-74 years. The two most important visual complications of diabetic retinopathy are diabetic macular edema (DME) and proliferative diabetic retinopathy (PDR). The occurrence of retinal new vessels (NVs) represents an important risk factor for severe vision loss in patients with diabetes mellitus. About 60% of patients with proliferative diabetic retinopathy (PDR) respond to pan retinal photocoagulation (PRP) with regression of neovascularization within 3 months (**DRS 1981**). However, many patients require additional laser treatment and 4.5% ultimately require pars plana vitrectomy despite PRP (**Flynn et al 1992**). Although severe central vision loss resulting from PDR can be prevented with PRP in most cases, this destructive, often painful, laser procedure may be associated with decreased peripheral vision and increased risk of macular edema (**ETDRS 1991**).

Vascular endothelial growth factor (VEGF) has been implicated in the pathogenesis of human eye diseases characterized by neovascularization and blockage of VEGF has been associated with the inhibition of iris neovascularization and suppression of retinal NV formation in primates (**Aiello et al 1995, Adamis et al**

1996) and humans (**Avery 2006, Spaide & Fisher 2006**). Several studies demonstrated that intravitreal injection of bevacizumab (IVB) resulted in marked regression of retinal and iris neovascularization, and rapid resolution of vitreous hemorrhage in patients with PDR (**Arevalo et al 2009**). But this effect appears to be transient and reinjection is required after 12 weeks. In addition, IVB injection was demonstrated to be an effective adjunctive treatment to PRP in the treatment of PDR. Intravitreal bevacizumab injection before PRP was found to be beneficial in preventing PRP-induced visual dysfunction and foveal thickening and was associated with a greater reduction in the area of active leaking new vessels than PRP alone in patients with PDR (**Tonello et al 2008 , Cho et al 2009**).

Therefore, in the present study, we aim at compare the possible synergistic effects of intravitreal bevacizumab when used in combination with PRP to the effect of PRP alone in the treatment of patients with PDR.

Aim of the work

To evaluate the effects of pan retinal photocoagulation (PRP) alone compared with PRP plus intravitreal injection of 1.25 mg of bevacizumab regarding regression of new vessels and possible complications.

Patients and methods

Thirty eyes with PDR will be included into this clinical trial, which will be randomly divided into two groups; group (1) patients will receive PRP only and in group (2) will receive PRP plus Intravitreal bevacizumab injection of 1.25 mg in 0.05 ml.

-Inclusion criteria:

Patients with proliferative diabetic retinopathy.

-Exclusion criteria:

1. Central macular thickness more than 300 um.
 2. Ischemic type of macular edema.
 3. Previous PRP.
 4. Recent intraocular surgeries or intravitreal injections within the last 3 months.
 5. Media opacity (eg. corneal opacity, cataract, vitreous hemorrhage) that interferes with the proper evaluation of the posterior segment.
 6. Contraindications to fluorescein angiography (pregnancy, allergy to fluorescein dye, renal failure).
 7. Retinal detachment.
- Chosen patients will be subjected to :-
- a- Detailed general and ocular history.

- b- Full ophthalmological examination including BCVA, slit-lamp examination, and fundus biomicroscopy.
- c- Baseline Fundus fluorescein angiography.
- d- Baseline Optical coherence tomography to measure central macular thickness.
- e- Treatment will be applied as follows:
 - Group 1: PRP as recommended by ETDRS (1200 to 1600 burns of moderate intensity, 500- μ m size, one-half to one spot diameter spacing at 0.1 second duration, divided over at least two sessions).
 - Group 2: Intravitreal injection of bevacizumab (1.25 mg in 0.05 ml) one week before starting PRP (same settings as group 1).
- f- Follow up by:
 - Change in log MAR BCVA.
 - Change in total area of fluorescein leakage from new vessels in fluorescein angiography at the weeks 4 and 12.
 - OCT to measure change in the central macular thickness at the weeks 2, 4 and 12.

REVIEW
OF LITERATURE