# Evaluation of the Efficacy of Intravitreal Triamcinolone Acetonide Injection as an Adjuvant Therapy to Panretinal Photocoagulation in the Treatment of Proliferative Diabetic Retinopathy

A thesis submitted in partial fulfillment of the requirements for the **M.D** degree in **Ophthalmology**

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# Abstract

## Purpose:

This study was designed to evaluate the efficacy of combined intravitreal triamcinolone acetonide injection with panretinal photocoagulation in the treatment of proliferative diabetic retinopathy as compared with standard panretinal photocoagulation.

## Design:

This study is a prospective, comparative, non-randomized study.

## Setting:

Cairo University Hospitals (Kasr El-Aini Teaching Hospital, New Kasr El-Aini Hospitals); Ophthalmic surgical and laser units.

## Patients and Methods:

The study was carried out on 40 eyes with proliferative diabetic retinopathy. They were randomly divided into 2 groups. Group A (20 eyes of 18 patients) were treated with panretinal photocoagulation only. Group B (20 eyes of 14 patients) received intravitreal injection of triamcinolone acetonide followed one week later by panretinal photocoagulation. In group A, laser burns were applied over the entire retina-sparing the central macular area- over 2-3 sessions, 1 week apart. Focal macular photocoagulation (for the microaneurysms) was performed in the first session. In group B, intravitreal triamcinolone acetonide 0.1 ml (4 mg) was injected at the pars plana followed 1 week later by panretinal photocoagulation as in group A.

## The Main Outcome Measures:

These include best corrected visual acuity, fundus examination for the presence of neovessels and fundus fluorescein angiography for the site, size and number of neovessels. The examination was done before the start of treatment. After treatment, patients were first examined after 2 weeks as regards the best corrected visual acuity and fundus examination, and then at 1, 3 and 6 months thereafter. Fundus fluorescein angiography was done before treatment, and then at one month, three months and six months after treatment. The results were statistically analyzed.

## Results:

***In group A:***
At 6 months after treatment, the best corrected visual acuity ranged from counting fingers 1m to 0.6, 3 of the 6 eyes with neovessels at the disc showed recurrence and the other 3 eyes showed complete regression of the neovessels. All the 19 eyes with neovessels elsewhere showed complete regression on fundus fluorescein angiography.

***In group B:***
At 6 months after treatment, the best corrected visual acuity ranged from counting fingers 1m to 0.9, 1 of the 8 eyes with neovessels at the disc showed no response to treatment while the other 7 eyes showed complete regression of the neovessels. Only 2 of the 18 eyes with neovessels elsewhere still showed leakage on fundus fluorescein angiography in one area while the other 16 eyes showed complete regression of the neovessels.

## Conclusion:

Intravitreal triamcinolone acetonide is a safe and effective accelerating adjuvant therapy to panretinal photocoagulation in the treatment of proliferative diabetic retinopathy. It speeds the regression of the neovessels through its anti-angiogenic action and speeds the improvement of visual acuity in patients with concomitant diabetic macular edema through its anti-inflammatory action. However, further studies on larger groups for longer follow-up periods are required to support the conclusions.

## Key Words:

Intravitreal triamcinolone acetonide, panretinal photocoagulation, proliferative diabetic retinopathy, anti-angiogenesis, fundus fluorescein angiography.

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# List of Abbreviations

ADA: American Diabetes Association

ARMD: Age Related Macular Degeneration

BCVA: Best Corrected Visual Acuity

BRB: Blood Retinal Barrier

CF: Counting Fingers

CMT: Central Macular Thickness

CNV: Choroidal Neovascular Membrane

CSME: Clinically Significant Macular Edema

CWS: Cotton Wool Spots

D: Diopters

DA: Disc Area

DCCT: Diabetes Control and Complications Trial

DD: Disc Diameter

DM: Diabetes Mellitus

2, 3 DPG: 2, 3 Di-Phospho Glycerate

DR: Diabetic Retinopathy

ETDRS: Early Treatment Diabetic Retinopathy Study

FFA: Fundus Fluorescein Angiography

FGF-2: Fibroblastic Growth Factor 2

G: Gauge

H: Hemorrhage

Hg A1C: Glycosylated Hemoglobin

IDD: Insulin-Dependent Diabetes

IgG1: Immunoglobulin G1

IL-6: Interleukin-6

IOP: Intra-Ocular Pressure

IRMA: Intra Retinal Micro-vascular Abnormalities

IV: Intra-Venous

IVTA: Intravitreal Triamcinolone Acetonide

KDR: Kinase insert Domain Receptor

LogMAR: logarithm of the Minimum Angle of Resolution

µ: Micron

m: Meter

Ma: Micro-aneurysm

mg: Milligram

MGP: Macular Grid Photocoagulation

ml: Milliliter

MLG: Macular Laser Grid

mm: Millimeter

mmHg: Millimeter Mercury

mW: Milli-Watt

MW: Molecular Weight

NADPH: Nicotinamide Adenine Dinucleotide Phosphate Hydrogen

NIDD: Non-Insulin Dependent Diabetes

NPDR: Non-Proliferative Diabetic Retinopathy

NVDS: Neo Vessels at Disc

NVEs: Neo Vessels Elsewhere

OCT: Optical Coherence Tomography

OD: Oculus Dexter

OS: Oculus Sinister

PDR: Proliferative Diabetic Retinopathy

PDT: Photo Dynamic Therapy

PED: Pigment Epithelium Defect

PG: Prostaglandin

PGI-2: Prostacyclin

PRP: Pan Retinal Photocoagulation

P-value: Probability Value

PVD: Posterior Vitreous Detachment

RD: Retinal Detachment

RPCs: Radial Peripapillary Capillaries

RPE: Retinal Pigment Epithelium

SD: Standard Deviation

SPSS V20.0: Statistical Package for Social Sciences Version 20.0

TA: Triamcinolone Acetonide

TRD: Tractional Retinal Detachment

TXA-2: Thromboxane A-2

UCVA: Uncorrected Visual Acuity

UKPDS: United Kingdom Prospective Diabetes Study

VB: Venous Beading

VEGF: Vascular Endothelial Growth Factor

WHO: World Health Organization

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# Introduction

Diabetic retinopathy is the most common cause of blindness in adults in all industrialized countries. [1]

The standard treatment of proliferative diabetic retinopathy is panretinal photocoagulation, which improves the visual prognosis in diabetic patients. However, the visual acuity and grade of retinopathy before treatment are known indicators of the visual prognosis after treatment. [2]

Triamcinolone acetonide is a steroid now being applied in a variety of retinal disorders; commonly through an intravitreal injection. The spectrum of ocular indications in which intravitreal triamcinolone acetonide may be therapeutically useful has recently been expanding. [3]

Comparing the various diseases with respect to effects and side effects of treatment, the best response to triamcinolone acetonide regarding visual outcome has been achieved for intra-retinal edematous diseases. Examples include diffuse diabetic macular edema [4], branch retinal vein occlusion, central retinal vein occlusion, pseudophakic cystoid macular edema and non-infectious uveitis. [5]

Recently, intravitreal triamcinolone acetonide has been increasingly applied as treatment for various intraocular neovascular diseases. Some studies have suggested that intravitreal triamcinolone acetonide may be useful as an angiostatic therapy in eyes with iris neovascularization and proliferative ischemic retinopathies. [5]

It has been reported that intravitreal triamcinolone acetonide may be a useful adjuvant to scatter panretinal photocoagulation for florid proliferative diabetic retinopathy. [3]

A case report stated that intravitreal triamcinolone acetonide may also be useful in the treatment of optic nerve head neovascularization in patients with proliferative diabetic retinopathy. [6]

## Aim of Work:

The aim of this study is to evaluate the efficacy of combined intravitreal triamcinolone acetonide injection with panretinal photocoagulation in the treatment of proliferative diabetic retinopathy as compared with standard panretinal photocoagulation.

This study aims at trying to answer the following questions:

1. Is intravitreal triamcinolone acetonide a safe procedure?
2. Is it easy to perform?
3. Does it have an anti-angiogenic effect on retinal neovascularization in diabetic patients?
4. If so, how long does its effect last?
5. Does it provide a rapid visual rehabilitation?
6. What are the possible complications?

# Retinal Microcirculation

There are two sources of blood supply to the human retina; the central retinal artery and the choroidal blood vessels. [7]

Choroidal blood vessels supply the outer 1/3 of the retina (outer four layers) - particularly the photoreceptors - while the central retinal artery supplies the inner 2/3 of the retina. [8]

Choroidal capillaries are fenestrated, with pores covered by thin, permeable membranes. Such fenestrations result in high permeability to low molecular weight (MW) substances as glucose and small proteins as albumin. This high permeability is important in maintaining a high concentration of glucose to the retinal pigment epithelium (RPE) and transport of proteins involved in vitamin A cycle. Moreover, this high permeability helps in setting up an osmotic pressure gradient between the subretinal space and extravascular choroidal space which drives water from the former to the latter. [9]

The central retinal artery has four main branches (arterioles). These branches supply three layers of capillary networks: radial peripapillary capillaries (RPCs), inner capillary network and outer capillary network. [10]

The RPCs are the most superficial layer of capillaries, lying in the inner part of the nerve fiber layer (IX). They anastomose with each other and with the deeper capillaries. The inner capillaries lie in the ganglion cell layer (VIII) under and parallel to the RPCs. The outer capillaries lie in the inner nuclear layer (VI). [10]

The capillaries drain into precapillary venules, then into small and large venules and then into the central retinal vein. Venules are deeper to the arterioles. [10]

Macular vessels arise from the temporal branches of the central retinal artery. They form a single layer ring of vessels around the fovea surrounding the capillary free zone about 500 μm in diameter (foveal avascular zone). Another capillary free zone is also present around the arterioles (periarteriolar capillary free zone). [10]

The retinal vasculature around the fovea is illustrated in figure 1: [11]

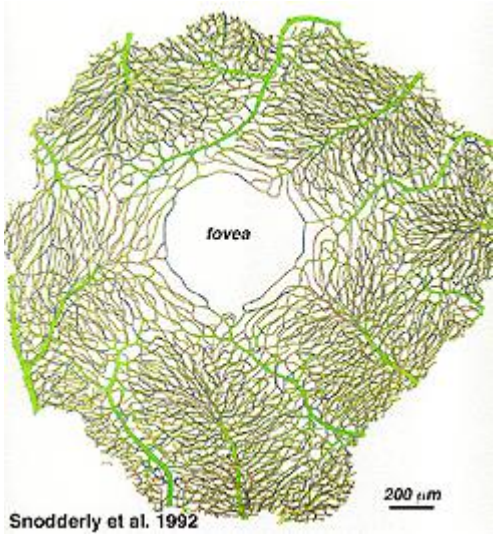


Fig. 1: [11]
Retinal vasculature around the fovea
in Rhesus monkey

The retinal capillaries are characterized by having a single layer of nonfenestrated (continuous) endothelium surrounded by a thick basement membrane within which is a discontinuous layer of intramural pericytes. Pericytes are pluripotent contractile cells which support the vessel wall and help protect it against changes in arterial blood pressure. Loss of the pericytes in diabetes mellitus contributes to the formation of microaneurysms. [12]

Tight junctions (zonula occludens) between the endothelial cells form the inner blood retinal barrier (BRB), the outer layer being represented by the tight junctions between the apices of the RPE. [13, 14]

A defect in the BRB exists at the anterior optic nerve where water-soluble substances as glucose and amino acids can diffuse from the extravascular space of the choroid to the anterior part of the optic nerve. Moreover, the capillaries of the prelaminar portion of the optic nerve are less tight than the retinal capillaries. [15]