Combined intravitreal triamcinolone acetonide injection and grid laser photocoagulation in treatment of diabetic macular edema

(Essay)

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By

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﴿قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا
إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ
الْعَلِيمُ الْحَكِيمُ﴾

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Mahmoud Ahmed Shafeek

Content

List of Abbreviations

AGEs	: Advanced Glycation End products
AMD	: Age related Macular Degeneration
BCVA	: Best Corrected Visual Acuity
BRB	: Blood Retinal Barrier
CMT	:Central Macular Thickness
CSME	: Clinically Significant Macular Edema
DDS	: Drug Delivery System
DME	: Diabetic Macular Edema
DRCR	: Diabetic Retinopathy Clinical Research
DR	: Diabetic Retinopathy
ELM	: External Limiting Membrane
ETDRS	: Early Treatment Diabetic Retinopathy Study
FAZ	: Foveal Avascular Zone
ICAM	: Inter-Cellular Adhesion Molecule
IGF-1	: Insulin like Growth Factor-1
ILM	: Internal Limiting Membrane
INL	: Inner Nuclear Layer
IOP	: Intra Ocular Pressure
IPL	: Inner Plexiform Layer
MMPs	: Matrix Metalloproteinases
NFL	: Nerve Fiber Layer
ONL	: Outer Nuclear Layer
OCT	: Optical Coherence Tomography

PDR :Proliferative Diabetic Retinopathy
OCT : Optical Coherence Tomography
OPL : Outer plexiform Layer
PEDF : Pigment Epithelium Derived Factor
PKC : Protien Kinase c
PPDR :Pre- proliferative Diabetic Retinopathy
PVD : Posterior Vitreous Detachment
RAGE :Receptor dependent effect Advanced Glycation End products
RESOLVE : Safety and Efficacy of Ranibizumab in Diabetic Macular Edema with Center Involvement
RPE : Retinal Pigmented Epithelium
SDM : Subthreshold Diode Micropulse
SRD : Serous Retinal Detachment
IVTA : Intra-Vitral Triamcinolone Acetonid
VA : Visual Acuity
VEGF : Vascular Endothelial Growth Factor
UKPDS : United Kingdom Prospective Diabetes Study

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Introduction

Diabetic macular edema (DME) is the leading cause of blindness in the diabetic population. Although its prevalence varies, the Diabetes Control and Complications Trial (DCCT) reported that 27% of type 1 diabetic (DM1) patients developed macular edema within nine years of onset **(White et al, 2012)**. Other studies indicate that in type 2 diabetic patients (DM2), prevalence increases from 3% within 5 years of diagnosis to 28% after 20 years **(klein et al, 1995).**

The Early Treatment Diabetic Retinopathy Study sponsored by the National Eye Institute in 1979 was a benchmark in the management of diabetic macular edema. Since publication of the Early Treatment Diabetic Retinopathy Study (ETDRS) findings the management of diabetic macular edema has been expanded.

At present, treatment options are quite broad, incorporating proven and new therapies or combinations of them, each designed to target a central patho- physiologic mechanism of the disease (**Antonopoulos et al, 2012).**

Three proven methods exist to decrease the long-term risk of vision loss from DME, namely:

(1) Tight blood sugar control;

(2)Blood pressure control;

(3) Focal laser photocoagulation therapy.

Mono-therapy:

Laser photocoagulation with a focal/grid laser can decrease vision loss from DME, however a number of patients fail to respond optimally to laser treatment **(Photocoagulation for diabetic macular edema 1985, Early photocoagulation for diabetic macular edema 1991-98), (Schachat 2008)**.

Inflammatory processes may be an important component of retinal damage in DME **(Antonetti et al, 1989)**, which has led to investigation of intravitreal corticosteroids as a possible treatment **(Nauck et al, 1998), (Antonetti et al , 2002), (Edelman et al , 2005).**

Studies suggest intravitreal dexamethasone improves visual acuity and central macular thickness **(Kuppermann et al, 2007), (Haller et al, 2010)**.

Adverse effects of intravitreal steroids include glaucoma and cataract formation **(Jonas et al, 2003), (Diabetic Retinopathy Clinical Research Network, 2008).**

Vascular endothelial growth factor (VEGF) is another proposed culprit for damage in DME, possibly via increased vascular permeability and action as a proinflammatory mediator **(Roberts et al, 1995), (Lutty et al, 1996).**

Combined therapy:

Intravitreal Triamcinolone acetonide injection plus Macular laser photocoagulation, Intravitreal Anti-VEGF plus Macular Laser Photocoagulation, or Intravitreal Anti-VEGF plus Corticosteroids all used as combined therapy.

Macular laser photocoagulation decreases oxygen consumption by destroying photoreceptors. Hence, combining anti-VEGF with laser photocoagulation is a complementary treatment with high efficacy in treating DME and decreasing recurrence.

Combination therapy of IVTA plus macular laser is more effective than either mono-therapy and may be comparable to anti-VEGF plus laser photocoagulation. The success of this combination therapy may be due to several mechanisms: IVTA decreases foveal thickness and allows more precise and effective macular laser photocoagulation with lower energy levels needed. Furthermore, steroids might promote the formation of mature laser scars.

A deterioration of macular edema is a well-known complication of laser treatment. Intravitreal therapeutic levels of steroids seem to be protective and even modulate the RPE modeling after laser **(Zur et al, 2012).**

Patients with intractable diabetic macular edema did not experience significant improvement in visual acuity after

therapy with bevacizumab/dexamethasone or pegaptanib/dexamethasone. However, decreased central macular thickness was seen after both therapies **(Leitner et al, 2012).**

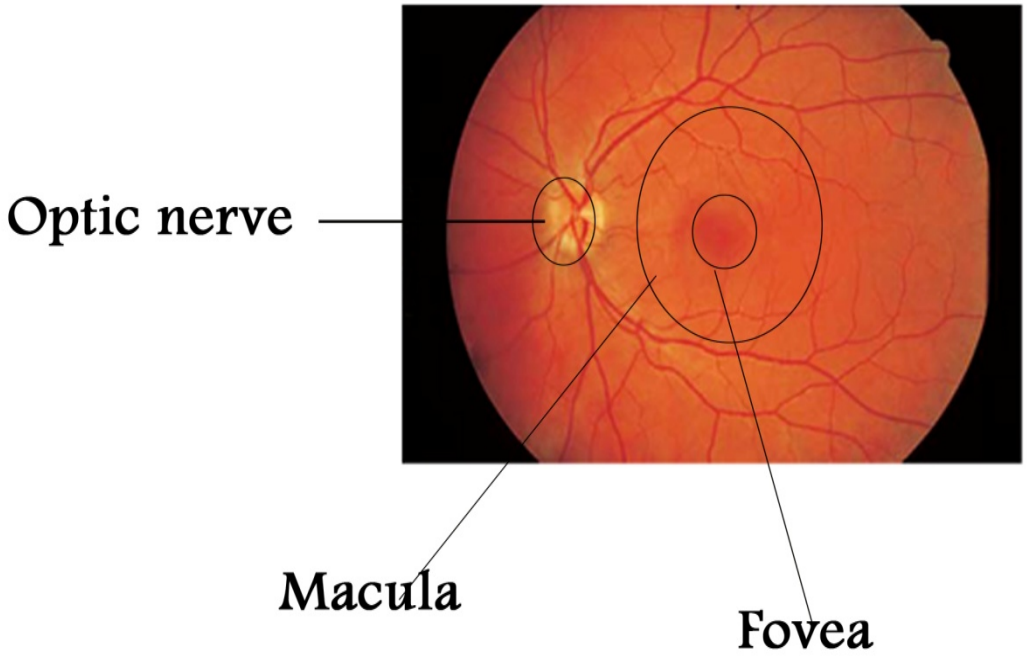
Aim Of The Work

To review the literature as regards the efficacy of combined triamcinolone acetonide injection and grid laser photocoagulation for treatment of diabetic macular edema.

ANATOMY OF THE MACULA

Macroscopic anatomy:

Anatomically the macula (macula lutea or central retrina) is defined as that central portion of the posterior retina that is enclosed between the temporal arcades. It measures approximately 5.5 mm in diameter and is centered approximately 4 mm temporal to and 0.8 mm inferior to the center of the optic disc **(Fig. 1) (Gass et al, 1997), (Lang et al, 2000).**

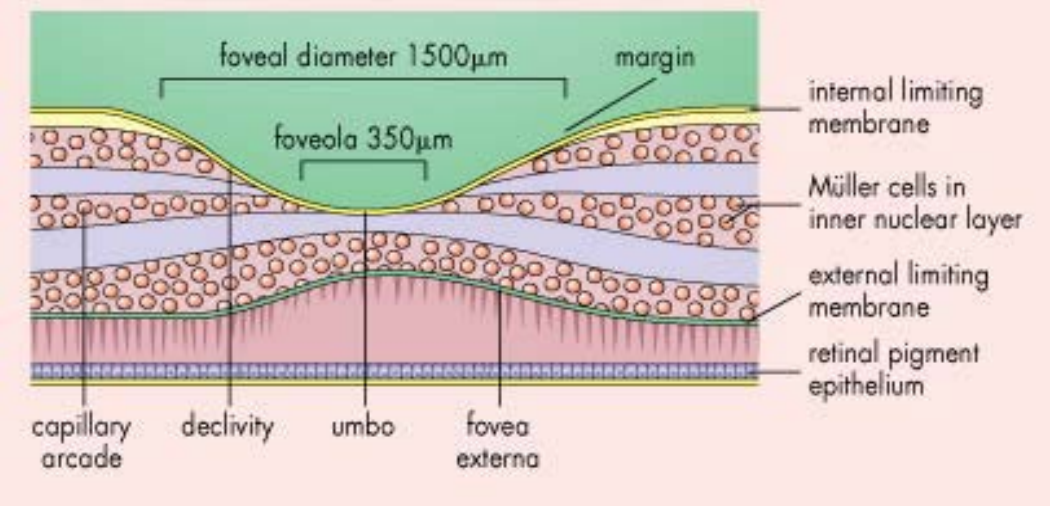


(Fig.1) Normal fundus (a: optic nerve, b: fovea) **(Lang et al, 2000).**

The macular area can be subdivided into several zones:

- **Fovea**: Which marks the approximate center of the area centralis is located at the posterior pole of the globe, 4 mm

temporal to the center of the optic disc and about 0.8 mm below the horizontal meridian, It has a diameter of 1.85 mm (which represents 5 degrees of the visual field) and an average thickness of 0.25 mm, At the center of the fovea, the layers of the retina are thinner so that a central concave indentation is present, the foveola produces the downward sloping border which meets the floor of the foveal pit and is known as the clivus, as shown in (**Fig. 2), (McDonnel et al, 1994).**



(Fig.2) Normal macular histology (Sigelaman et al, 1982).

- **Foveola:** It forms the central floor of the fovea and has a diameter of 0.35 mm. It is devoid of ganglion cells. Histoloically, it is the part of the retina where cones photoreceptors are concentrated at maximum density. The only other elements present are the retinal pigment epithelium and the cytoplasmic processes of Müller cells, which form the inner and outer limiting membranes. It