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Tamer Fahmy Eliwa

List of Abbreviations

ACE	:	Angiotensin converting enzyme .
a FGF	:	Acidic fibroblast growth factor
AGE	:	Advanced glycation end product
Ang II	:	Angiotensin II
Ang2	:	Angiopiotin2
ANP	:	Atrial natriuretic peptide
AR	:	Aldose reductse
ARBs	:	Angiotensin receptor blockers
AT1-R	:	Angiotensin II type 1 receptor.
AT-II	:	Angiotensin II
bFGF	:	Basic fibroblast growth factor
CF	:	Counting fingers
CFZ	:	Capillary free zone
CLBM	:	Contact lens slit lamp biomicroscopy
CME	:	Cystoid macular edema
CMT	:	Central macular thickness
CSME	:	Clinically significant macular edema
DAG	:	Diacylglycero
DCCT	:	Diabetic control and complication trial.
DHAP	:	Dihydroxyacetone phopsphate
DME	:	Diabetic macular edema
DRS	:	Diabetic Retinopathy Study Research Group
ELM	:	External limiting membrane.
eNOS	:	Endothelial nitric oxide synthase
EPC	:	Endothelial progenitor cells
ET-1	:	Endothelin-1
ETDRS	:	Early treatment Diabetic Retinopathy Study Group
F-6P	:	Fructose-6-phosphate
FAZ	:	Foveal avascular zone.
FFA	:	Fundus flouresciene angiography

List of Abbreviations (Cont.)

FGF	:	Fibroblast growth factor
G1cN	:	Glucosamine
G1cN-6P	:	Glucosamine-6-phosphate
G-6P	:	Glucose-6-phosphate
GA-3P	:	Glyceraldehyde-3 -phosphate
GA-3PD	:	Glyceraldehyde-3 -phosphate dehydrogenase
GFAT	:	Glucosamine-fructose-amidotransferase
GK	:	Glucokinase
HGF	:	Hepatocyte growth factor.
HIFs	:	hypoxia-inducible factors
HM	:	Hand Motion
HRE	:	Hypoxia response element
ICAM-1	:	Intercellular adhesion molecule-1
IL-6	:	Interleukin-6.
ILM	:	Inner limiting membrane
INL	:	Inner nuclear layer
IPL	:	Inner plexiform layer
IRMA	:	Intraretinal microvascular abnormalities
IVFA	:	Intravenous fluorescein angiogram
IVTA	:	Intravitreal injection of triamcinolone acetonide.
K	:	Hexokinase
MMP-9	:	Matrix metal-proteinase-9
NO	:	Nitric oxide
NPDR	:	Non-proliferative diabetic retinopathy
NV	:	Neovessels
NVI	:	Neovessels at iris
OCT	:	Optica coherence tomography
ONH	:	Optic nerve head
ONL	:	Outer nuclear layer
OPL	:	Outer plexiform layer

List of Abbreviations (Cont.)

PA	:	Plasminogen activator
PAI-1	:	Plasminogen activator inhibitor-1
PDGF	:	Platelet derived growth factor
PDGF	:	Platelet-derived growth factor
PDR	:	Proliferative diabetic retinopathy
PEDF	:	Pigment epithelial derived factor
PG	:	Postaglandins
PHT	:	Posterior hyaloid traction.
PKC	:	Protein kinase C
PL	:	Perception of light
R-5P	:	Ribose-5phosphate
RAGE	:	Receptor for advanced glycation endproducts
ROS	:	Reactive oxygen species
RPE	:	Retinal pigment epitheluim
SD	:	Sorbitol dehydrogenase
SDF-1	:	Stromal derived factor-1
SDM	:	Subthreshold diode micropulse
SLO	:	Scanning laser ophthalmoscope
TA	:	Triamcinolone acetonide
TGF	:	Transforming growth factor
TNFα	:	Tumor necrosis factor α
TX	:	Thromboxane
UKPDS	:	United Kingdome Prospective Diabetes Study
USA	:	United State of America
VA	:	Visual acuity
VCAM-1	:	Vscular cellular adhesion molecule-1
VEGF	:	Vascular endothelial growth factor
VEGFR2	:	VEGF-receptor 2
WESDR	:	Wisconsin Epidemiologic Study of Diabetic Retinopathy

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AIM OF THE WORK:

To study, evaluate & compare the efficacy of retreatment by laser photocoagulation versus intravitreal injection of triamcinolone acetonide in treatment of refractory diabetic macular edema.

INTRODUCTION

Diabetic retinopathy is one of the most common causes of macular edema. The prevalence of macular edema is 3% in people with mild non-proliferative diabetic retinopathy (NPDR); 38% in those with moderate to severe NPDR; and 71% in those with PDR ***(Klein et al, 1984b).***

Diabetic macular edema (DME) is the result of retinal microvascular changes that occur in diabetic patients. Thickening of the basement membrane of retinal capillaries and reduction in the number of pericytes are believed to lead to increased permeability and incompetence of retinal vasculature. This compromise of blood-retinal barrier leads to the leakage of plasma constituents in the surrounding retina, resulting in retinal edema ***(Khan & Wai-Ching, 2001).***

Diabetic patients with macular edema usually complain of blurring of vision. 25-30% of patients with clinically significant macular edema (CSME) exhibit doubling of the visual angle within 3 years. Diabetic macular edema is best diagnosed by slit-lamp biomicroscopy which appears either as focal edema due to leakage from microaneurysms or as diffuse edema due to breakdown of blood-retinal barrier

with leakage from micro aneurysms, retinal capillaries, and arterioles ***(Khan & Wai-Ching, 2001).***

Imaging studies are useful in confirming macular edema like fluorescein angiography, which is used to distinguish and localize areas of focal versus diffuse leakage, thereby guiding the placement of laser photocoagulation. It is helpful to exclude ischemic macular edema ***(Kylstra et al, 1999).***

Optical coherence tomography (OCT) has been able to measure central macular thickness, and also demonstrate 3 basic structural changes of the retina in DME, i.e., retinal swelling, cystoid edema, and serous retinal detachment ***(Otani et al, 1999).***

Laser treatment is clearly the first-line treatment of DME in order to reduce progression & the risk of doubling the visual angle from 24% to 12%, over all levels of visual acuity, over a period of 3 years ***(ETDRS, report no.1, 1985).*** Unfortunately, even with well-timed and adequate laser treatment, many patients continue to lose vision ***(Martidis et al, 2002).***

Recent research in pharmacotherapy for diabetic retinopathy and macular edema offers new hope for these difficult situations. Steroids are a class of medications

being studied with intense interest for the treatment of diabetic macular edema. They are known to be effective for the treatment of inflammatory types of macular edema, such as uveitis or pseudophakic cystoid macular edema (CME) ***(Martidis et al, 2002)***.

Steroids are potent anti-inflammatory agents. They are thought to inhibit production of vascular endothelial growth factor and have been shown to decrease the breakdown of the blood-retinal barrier. These qualities make steroids a potential treatment in diabetic retinopathy ***(Wilson et al, 1992 & Martidis et al, 2002).***

Martidis & his associates in 2002 did a prospective study on intravitreal injection of triamcinolone acetonide in refractory diabetic macular edema & their results were satisfactory. These findings are confirmed by significant decrease in fluoresceine leakage within the macula & leakage from retinal neovascularization ***(Brooks et al, 2004 and Avci, Kaderli and Akalp, 2006).***

ANATOMY OF THE MACULA

THE RETINA:

Retina or nervous coat of the eye is a delicate diaphanous tissue that varies in thickness: 0.13mm at the umbo, 0.56mm at the foveal margin and adjacent to the optic nerve head (ONH), 0.1mm at the ora and 0.2mm at equator ***(Gass, 1997).***

As seen in the cross-section by light microscopy, the retina is represented by 10 layers from outside inward they are: RPE, photoreceptor layer of rods and cones, external limiting membrane, outer nuclear layer(ONL), outer plexifrom layer(OPL), inner nuclear layer(INL), inner plexifrom layer(IPL), ganglion cell layer, nerve fiber layer and internal limiting membrane ***(Yanoff and Duker, 2003).***

THE HUMAN MACULA:

- *Anatomical consideration:*

Anatomically, the macula (macula lutea or central retina) is defined as that portion of the posterior retina that contains xanthophyll and two or more layers of ganglion cells. It measures approximately 5.5mm in diameter and is centered approximately 4mm temporal to and 0.8mm inferior to the center of the optic disc**.** It corresponds to approximately 15 degree of the visual field ***(Gass, 1997).***