

MANAGEMENT OF AGE RELATED MACULAR DEGENERATION

Essay
Submitted for partial fulfillment of
M.Sc. in Ophthalmology

By
Hend Mohamed Abd Alla Belal
M. B., B. CH.

Supervised by

Prof. Dr. Ismail Hamza
Professor of Ophthalmology
Faculty of Medicine
Ain Shams University

DR. Amr I. El Awamry
Lecturer of Ophthalmology
Faculty of Medicine
Ain Shams University

Faculty of Medicine
Ain Shams University
Cairo 2010

Acknowledgment

In the name of God the most Gracious, the most Merciful, whom I would like to thank for all his blessings in my life and throughout this work.

I would like to express my almost thanks and greatest gratitude to Prof. Dr. Ismail Hamza for his support, guidance and valuable advice.

I would also like to express my deepest thanks to Dr. Amr I. El Awamry for his help, valuable ideas and precious time.

I would also like to express my almost thanks and greatest gratitude to Prof. Dr. Ahmed Abo Al Enin for his support and guidance.

Last but not least I would like to thank my family for their support and suffering throughout this work.

List of Contents

List of Figures	III
List of Tables.....	IX
List of Abbreviations.....	X
Aim of Work	XIV
Introduction	1
<u>Chapter 1: Anatomy</u>	
Anatomy of the macula	5
Choroid and blood supply of the retina.....	6
<u>Chapter 2: Pathology of AMD</u>	
Pathology of AMD	10
Pathogenesis of Choroidal Neovascular membrane.....	15
<u>Chapter 3: Clinical features of AMD</u>	
Epidemiology and Risk factors of AMD	17
Clinical features of Age Related Macular Degeneration	25
<u>Chapter 4: Investigations of AMD</u>	
Fluorescein Angiography.....	32
Indocyanin Green Angiography	45

List of Figures

Scanning Laser Ophthalmoscope- based Angiography	50
Optical Coherence Tomography	52
Multi-focal ERG.....	63
Analysis of the drusen	64

Chapter 5: Treatment Modalities of AMD

Antioxidants	67
Laser photocoagulation	71
Photodynamic Therapy	79
Transpupillary Thermotherapy.....	91
Pharmacotherapy	95
Radiation Therapy	137
Gene Therapy	139
Retinal Pigment Epithelial Transplantation	140
Electronic Implants.....	144
Macular Translocation.....	145
Submacular Surgery	152
Summary	160
References	162
Arabic summary... ..	196

List of Figures

(1) Cross section of the fovea.....	5
(2) Anatomy of Bruch`s membrane	8
(3) Pathogenesis of age related macular degeneration	13
(4) Choroidal neovascular membrane in cross section	15
(5) Age and Macular Degeneration.....	18
(6) Picture seen by Age Related Macular Degeneration patient..	25
(7) Amsler Grid as it appears to patient with AMD.....	26
(8) Classification of AMD.....	27
(9) Hard drusen and Soft drusen	27
(10) Calcified drusen	28
(11) RPE Pigmentation.....	28
(12) Geographic atrophy	29
(13) Early and end stage AMD classic CNV and Occult CNV	30
(14) Late AMD.....	30
(15) Late AMD	31

List of Figures

(16) Hard drusen in FA	33
(17) Hard drusen in FAIV	34
(18) Soft drusen in FA.....	35
(19) Geographic atrophy in FA	36
(20) Geographic atrophy in FA	37
(21) Predominantly classic CNV in FA	38
(22) Minimally classic CNV in FA.....	39
(23) CNV temporal to the fovea.....	40
(24) Subfoveal CNV.....	40
(25) Juxtafoveal CNV	40
(26) Classic CNV in FA	41
(27) Occult CNV in FA.....	42
(28) PED in FA.....	43
(29) CNV in FA and ICG	46
(30) Classic CNV in ICG	47
(31) Occult CNV in ICG	48
(32) AMD with CNV in ICG	49
(33) Normal OCT	53

List of Figures

(34) Soft drusen in OCT.....	54
(35) Confluent soft drusen in OCT	55
(36) Atrophic AMD with foveal sparing.....	56
(37) Exudative AMD, indirect signs	57
(38) Increased retinal thickness.....	58
(39) Diffuse retinal thickness	59
(40) PED.....	59
(41) Occult with no classic CNV	60
(42) Fibrovascular PED.....	61
(43) Occult CNV with PED	62
(44) m-focal ERG	64
(45) Isolation of the drusen	65
(46) Extensive, confluent drusen.....	71
(47) Diode laser treatment.....	73
(48) Pre- and post-laser images.....	75
(49) Managing CNV using conventional laser.....	76
(50) Pre- and post-laser images using trans-scleral diode laser	78
(51) Photodynamic therapy for macular degeneration.....	79

List of Figures

(52) Verteporfin: pharmacological structure.....	80
(53) PDT ttt spot size for large CNV	83
(54) PDT ttt spot size for small CNV.....	84
(55) Algorithm for Verteporfin therapy for neovascular AMD	88
(56) Algorithm for monitoring, performing FA and retreatment.....	89
(57) Prephotodynamic therapy fluorescein angiography	89
(58) Pre-and post- TTT	93
(59) Pre- and post- transpupillary thermotherapy	95
(60) Triamcinolone acetonide formula.....	97
(61) Fifty-year-old patient visual acuity prior to intravitreal triamcinolone acetonide.....	98
(62) Combined treatment	101
(63) Patient receive only PDT	102
(64) PDT with TA	103
(65) TA delivery	105
(66) VEGF isoforms.....	112
(67) Role of the VEGFR tyrosine kinases in endothelial cell..	114

List of Figures

(68) Ribbon representation of the VEGFVEGFR1- domain 2 complex.....	114
(69) VEGF pathway	115
(70) Treatment strategies for choroidal neovascularization...	116
(71) Patient before and after treatment with bevacizumab. ...	119
(72) Patient before and after treatment with bevacizumab. ...	120
(73) Minimally classic lesion before and after treatment with bevacizumab	120
(74) Examples of optical coherence therapy (OCT) images from different patients being treated with ranibizumab .	124
(75) Antisense molecules bind mRNA	128
(76) Triple therapy.....	132
(77) Serial OCT images in a patient with neovascular AMD before and 2 months after the first intravitreal injection of 1 mg of infliximab	134
(78) Serial OCT images before, 2 months after the first intravitreal 2 mg infliximab.....	135
(79) OCT images before the first intravitreal 2 mg infliximab	136
(80) Subfoveal CNV and radiation therapy	138
(81) Patient received translocated IPE cells after removal of the CNV	143

List of Figures

(82) The Implantable Miniature Telescope.....	144
(83) The head in an upright position following the surgery ..	147
(84) Three days following inferior limited macular translocation	148
(85) Macular translocation technique applied in rabbits.....	149
(86) Macular translocation for subfoveal choroidal neovascularization	151
(87) Retinotomy site.....	154
(88) Creation of a small neurosensory retinal detachment..	155
(89) Horizontal subretinal forceps.....	155

List of Tables

(1) Epidemiology of AMD	17
(2) Major molecular constituents of drusen	66
(3) The treatment parameters for direct treatment of CNV	76
(4) Angiogenic and angiostatic factors	108
(5) Different between Macugen, Lucentis and Avastin	126

 List of Abbreviations

List of Abbreviations

ABMES	Australian Blue Mountains Eye Study
AC	Anterior chamber
AMD	Age related macular degeneration
ANCHOR	Anti-VEGF Antibody for Treatment of Predominantly Classic Choroidal Neovascularization in AMD Antibody Ranibizumab In the Treatment of Neovascular AMD
AREDS	Age Related Eye Disease Study
BDES	Beaver Dam Eye Study
BLSA	Baltimore Longitudinal Study of Aging
BMES	Blue Mountains Eye Study
BMI	Body Mass Index
BPD	Benzoporphyrin Derivative
BPD-MA	Benzoporphyrin Derivative Monoacid
BSS	Balanced Salt Solution
CFH	Complement factor H
CLEAR	Clinical Evaluation of Anti-angiogenesis in the Retina
CNV	Choroidal Neovascular Membrane
DBP	Diastolic blood pressure

 List of Abbreviations

DHA	Docosahexaenoic Acid
DHE	Dihematoporphyrin Ether
ECM	Extracellular matrices
EDCC	Eye Disease Case Control Study
FA	Fluorescein Angiography
FAZ	Foveal A vascular Zone
FDA	Food and Drug Administration
FGF	Fibroblast Growth Factor
FOCUS	RhuFab V2 Ocular treatment combining the use of visudyne To evaluate safety Study
GLD	Greatest Linear Dimension
HGF	Hepatocyte Growth Factor
HPD	Hematoporphyrin Derivatives
HRA	Heidelberg Retinal Angiography
ICAM	Intercellular Adhesion Molecule
ICG	Indo Cyanine Green
IF-α	Interferon Alpha
IGF-1	Insulin-like Growth Factor
IL-8	Interleukin-8
INF	Interferon
IOP	Intraocular Pressure
IPE	Iris Pigment Epithelium
IVTA	Intravitreal Triamcinolone Acetonide



List of Abbreviations

LALES	Los Angeles Latino Eye Study
LDH	Low Density Lipoprotein
LSD	Laser Spot Size
MAC	Membrane Attack Complex
MARINA	Minimally Classic/ Occult Trial of the Anti-VEGF
MfERG	multi-focal electroretinogram
MPS	Macular Photocoagulation Study
MTS	Macular Translocation
NFL	Nerve Fiber Layer
NHANES	National Health and Nutrition Examination Survey
OCT	Optical Coherence Tomography
OPP	Ocular perfusion pressure
PAI-1	Plasminogen Activator Inhibitor type-1
PDGF	Platelet Derived Growth Factor
PDT	Photodynamic Therapy
PED	Pigment Epithelial Detachment
PEDF	Pigment Epithelial-Derived Factor
PEG	Polyethylene Glycol
PIGF	Placental Growth Factor

 List of Abbreviations

POLA	Pathologies Oculaires Liees a l'Age Study
RISC	RNA-induced silencing complex
RPE	Retinal pigment epithelium
SANA	Systemic Avastin for Neovascular AMD
SBP	Systolic blood pressure
SLO	Scanning Laser Ophthalmoscope
SNP	Single Nucleotide Polymorphism
TA	Triamcinolone Acetonide
TAP	Treatment of AMD with Photodynamic therapy
TGF	Transforming Growth Factor
TIA	Transient ischemic attack
TNF-α	Tumor necrosis Factor- α
t-PA	tissue Plasminogen Activator
TTT	Transpupillary Thermotherapy
VEGF	Vascular endothelial growth factors
VEP	Visual evoked potential
VIP	Verteporfin In Photodynamic therapy
VISION	VEGF Inhibition Study in Ocular Neovascularization