



شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكروفيلم

بسم الله الرحمن الرحيم



MONA MAGHRABY



شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكروفيلم



شبكة المعلومات الجامعية التوثيق الإلكتروني والميكروفيلم



MONA MAGHRABY



شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكروفيلم

جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات



يجب أن

تحفظ هذه الأقراص المدمجة بعيدا عن الغبار



MONA MAGHRABY

**Efficacy of posterior sub-Tenon's capsule injection
compared to intravitreal injection of triamcinolone
acetonide for treatment of diabetic macular edema:
A systematic review and meta-analysis**

Submitted for partial fulfillment of Master degree
in Ophthalmology

By

Mohamed Hamdy Ghazy Ibrahim

M. B., Bch., Faculty of Medicine, Ain Shams University

Under Supervision of

Prof. Dr. Abdelrahman Gaber Salman

Professor of Ophthalmology
Faculty of Medicine, Ain Shams University

Prof. Dr. Azza Mohamed Ahmed Said

Professor of Ophthalmology
Faculty of Medicine, Ain Shams University

Dr. Mariam Ahmad Al-Feky

Lecturer of Ophthalmology
Faculty of Medicine, Ain Shams University

Prof. Dr. Moustafa ELHusienni Moustafa

Professor Emeritus, Department of Community, Environmental
and Occupational Medicine
Faculty of Medicine, Ain Shams University

**Faculty of Medicine
Ain Shams University
Cairo – Egypt - 2020**

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قَالَ

لَسْبَحَانَكَ لَا عِلْمَ لَنَا
إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ
الْعَلِيمُ الْعَظِيمُ

صدق الله العظيم

سورة البقرة الآية: ٢٢



Acknowledgments

*First and foremost, I feel always indebted to **Allah**, the **Most Beneficent** and **Merciful**, Who gave me the strength to accomplish this work,*

*Words can never express my hearty thanks and indebtedness to **Prof. Dr. Abdelrahman Gaber Salman**, Professor of Ophthalmology, Faculty of Medicine, Ain Shams University, for his great support and continuous encouragement and guidance to complete this work. It was a great honor to work under his guidance and supervision.*

*I wish also to express my gratitude to **Prof. Dr. Azza Mohamed Ahmed Said**, Professor of Ophthalmology, Faculty of Medicine, Ain Shams University, for her valuable guidance and expert supervision, in addition to her great deal of support and encouragement. I really have the honor to complete this work under her supervision.*

*My deepest gratitude to my supervisor, **Dr. Mariam Ahmad Al-Feky**, Lecturer of Ophthalmology, Faculty of Medicine, Ain Shams University, for her great efforts, kind advice, support and encouragement throughout the whole work.*

*I would like to express my great and deep appreciation and thanks to **Prof. Dr. Moustafa ELHusienni Moustafa**, Professor emeritus, Department of Community, Environmental and Occupational Medicine, Faculty of Medicine, Ain Shams University, for his meticulous supervision, and his patience in reviewing and correcting this work.*

*✍ **Mohamed Hamdy Ghazy Ibrahim***



*Special thanks to my Parents, my
fiancé and all my Family members for
their continuous encouragement,
enduring me and standing by me.*

Contents

<i>Subject</i>	<i>Page No.</i>
List of Abbreviations.....	i
List of Figures	iv
List of Tables.....	vi
Introduction	1
Aim of the Study	6
Review of Literature	
Chapter (1): Diabetic Retinopathy	7
Chapter (2): Diabetic Macular Edema	22
Chapter (3): Management of Diabetic Macular Edema.....	32
Materials and Methods	58
Results.....	63
Discussion	104
Conclusion and Recommendations.....	112
Summary	114
References	117
Arabic Summary	—

List of Abbreviations

<i>Abbr.</i>	<i>Full-term</i>
ADA	: American Diabetes Association
AGEs	: Advanced glycation end-products
AGTR1	: Angiotensin II receptor Type 1
ANG II	: Angiotensin II
AQP4	: Aquaporin 4
BCVA	: Best corrected visual acuity
b-FGF	: Basic fibroblastic growth factor
BM	: Basement membrane
BMI	: Body Mass Index
BMPs	: Bone morphogenetic proteins
BRB	: Blood–retinal barrier
CI	: Confidence interval
CME	: Cystoid macular edema
CMT	: Central macular thickness
CSME	: Clinically significant macular edema
CYP	: Cytochrome P-450
DCCT	: Diabetes Control and Complications Trial
DD	: Disc diameter
DEX	: Dexamethasone
DF	: Degree of freedom
DISS	: Diabetes Incidence Study in Sweden
DM	: Diabetes mellitus
DME	: Diabetic macular edema
DR	: Diabetic retinopathy
DRCR	: Diabetic Retinopathy Clinical Research Network
DRT	: Diffuse retinal thickening
EGF	: Epidermal growth factor
ERM	: Epiretinal membrane
ETDRS	: Early Treatment of Diabetic Retinopathy Study
EUROD	: A collaboration of European Childhood Diabetes
IAB	Registers

FA	: Fluocinolone acetonide
FAZ	: Foveal avascular zone
FEM	: Fixed effect method
FFA	: Fundus Fluorescein Angiography
GFAP	: Glial fibrillary acid protein
ICAM-1	: Intercellular adhesion molecule-1
IDF	: International Diabetes Federation
IGF	: Insulin-like growth factor
ILs	: Interleukins
IOP	: Intraocular pressure
IVTA	: Intravitreal injection of triamcinolone acetonide
LCL	: Lower control limit
LDL	: Low-density lipoproteins
LEDGF	: Lens epithelium derived growth factor
MCP-1	: Monocyte chemoattractant protein-1
MD	: Mean difference
MLP	: Macular laser photocoagulation
MMPs	: Matrix metalloproteinases
Mo	: Month
NCD	: Non-communicable diseases
NF-κB	: Nuclear factor kappa-light-chain-enhancer of activated B cells
NPDR	: Non-proliferative diabetic retinopathy
OCT	: Optical coherence tomography
PDGF	: Platelet derived growth factor
PDR	: Proliferative diabetic retinopathy
PEDF	: Pigment epithelium derived factor
PGs	: Prostaglandins
PHT	: Posterior hyaloidal traction
PKC	: Protein kinase C
PIGF	: Placental growth factor
PRISMA	: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PRP	: Panretinal photocoagulation
PSC	: Posterior subcapsular cataract
RAGE	: Receptor for advanced glycation end products

RAS	: Renin-angiotensin system
RCTs	: Randomized controlled clinical trials
RD	: Retinal detachment
REM	: Random effect method
RNFL	: Retinal nerve fiber layer
ROS	: Reactive oxygen species
RPE	: Retinal pigment epithelium
SCS	: suprachoroidal space
SD	: Standard deviation
SE	: Standard error
SML	: Subthreshold micro-pulse laser
SRD	: Serous retinal detachment
STTA	: Posterior sub-Tenon's capsule injection of triamcinolone acetonide
T1DM	: Type 1 diabetes mellitus
T2DM	: Type 2 diabetes mellitus
TA	: Triamcinolone acetonide
TGF-β	: Transforming growth factor beta
TNF	: Tumor necrosis factor
UCL	: Upper control limit
UKPDS	: United Kingdom Prospective Diabetes Study
VA	: Visual acuity
VCAM-1	: Vascular cell adhesion molecule-1
VEGF	: Vascular endothelial growth factor
VH	: Vitreous hemorrhage
VLDL	: Very-low-density lipoprotein
VMI	: Vitreomacular interface
VMT	: Vitreomacular traction
WESDR	: Wisconsin Epidemiologic Study of Diabetic Retinopathy
WHO	: World health organization
WMD	: Weighted mean difference
ZO-1	: Zonula occludens-1

List of Figures

Figure No.	Title	Page No.
1	Pathologic changes in retinal neuro-vascular unit.	15
2	Progression of diabetic non-proliferative retinopathy.	16
3	The different pathways in the development of DR and DME.	21
4	Representative fundus images	26
5	(a) RPE alteration and mild swelling in the macula. (b) Hyperfluorescence in the macular region.	28
6	Optical coherence tomography appearance of morphological patterns of DME.	30
7	Optical coherence tomography appearance of VMI.	31
8	Focal photocoagulation burns grid photocoagulation burns.	34
9	PRP laser marks.	35
10	(A) Injection performed 3.5 mm from the limbus. (B) The eyelashes and the eyelids were completely draped.	42
11	(a) The anaesthetized conjunctiva is grasped with a pair of forceps and a tent is formed. (b) Tenon's capsule has been dissected in a blunt fashion through the aperture created.	49
12	Smith and Nozik method posterior sub-Tenon injection of triamcinolone acetonide.	50
13	Dexamethasone intravitreal implant and injector (Ozurdex).	53
14	Injection into the suprachoroidal space.	54
15	Flow diagram for systematic review (PRISMA checklist).	65

16	Forest plot of MD of the BCVA that targeted the IVTA and STTA groups at a one-month follow-up after the injection. MD is displayed on the x-axis.	72
17	Funnel plot of the BCVA log.MAR mean difference a one-month follow-up after the injection.	72
18	Forest plot of MD of the BCVA between that targeted the IVTA and STTA groups at a three-month follow-up after the injection.	75
19	Funnel plot of the BCVA log.MAR mean difference a three-month follow-up after the injection.	75
20	Forest plot of MD of the BCVA between that targeted the IVTA and STTA groups at a six-month follow-up after the injection.	78
21	Funnel plot of the BCVA log.MAR mean difference a six-month follow-up after the injection.	78
22	Forest plot of MD of the CMT that targeted the IVTA and STTA groups at a one-month follow-up after the injection.	82
23	Funnel plot of CMT μm mean difference a one-month follow-up after the injection.	82
24	Forest plot of MD of the CMT that targeted the IVTA and STTA groups at a three-month follow-up after the injection.	85
25	Funnel plot of the CMT μm mean difference a three-month follow-up after the injection.	85
26	Forest plot of MD of the CMT that targeted the IVTA and STTA groups at a six-month follow-up after the injection.	88
27	Funnel plot of the CMT μm mean difference a six-month follow-up after the injection.	88

28	Forest plot of MD of the IOP that targeted the IVTA and STTA groups at a one-month follow-up after the injection.	92
29	Funnel plot of the IOP mmHg mean difference a one-month follow-up after the injection.	92
30	Forest plot of MD of the IOP that targeted the IVTA and STTA groups at a three-month follow-up after the injection.	95
31	Funnel plot the IOP mmHg mean difference a three-month follow-up after the injection.	95
32	Forest plot of MD of the IOP that targeted the IVTA and STTA groups at a six-month follow-up after the injection.	98
33	Funnel plot the IOP mmHg mean difference a six-month follow-up after the injection.	98

List of Tables

Table No.	Title	Page No.
1	Excluded Randomized controlled trials.	66
2	Included Studies Characteristics.	67
3	Mean difference of BCVA in IVTA and STTA at baseline and one-, three-, and six-months.	68
4	Meta-analysis results of BCVA log.MAR mean difference a one-month follow-up after the injection.	70
5	Meta-analysis results of the BCVA log.MAR mean difference a three-month follow-up after the injection.	73
6	Meta-analysis results of the BCVA log.MAR mean difference a six-month follow-up after the injection.	76
7	Mean difference of the CMT in IVTA and STTA at baseline and one-, three-, and six-months.	79
8	Meta-analysis results of the CMT μm mean difference a one-month follow-up after the injection.	80
9	Meta-analysis results of the CMT μm mean difference a three-month follow-up after the injection.	83
10	Meta-analysis results of the CMT μm mean difference a six-month follow-up after the injection.	86
11	Mean difference of IOP for IVTA and STTA at baseline and one-, three-, and six-months.	89