Evaluation of the Macula, Retinal Nerve Fiber Layer and Choroid Thickness in Women Using Oral Contraceptive Pills

Thesis

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بسم الله الرحمن الرحيم

وَقُلِ اعْمَلُوا فَسَيَرَى اللَّهُ
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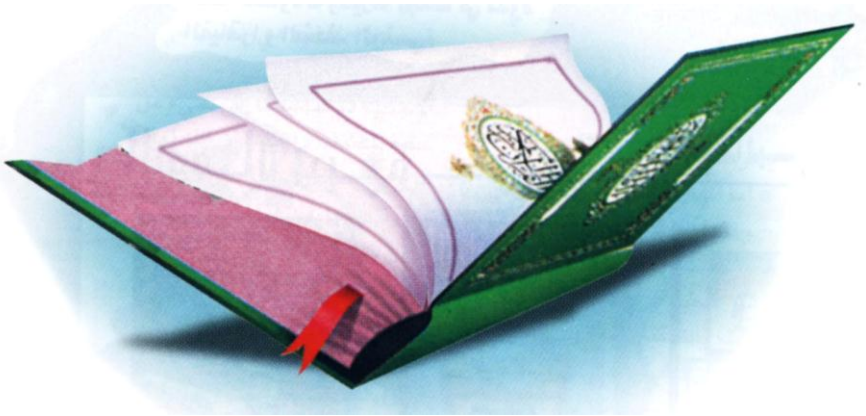

صدق الله العظيم

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Eman Magdy Gaber El-Said

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List of Abbreviations

Abb.	Full term
AMD	*Age-related macular degeneration*
Appt	*Activated partial thromboplastin time*
C/D	*Cup /Disc ratio*
COCS	*Combined oral contraceptive pills*
CPT	*Central point thickness*
CSF	*Central foveal subfield*
CT	*Choroid thickness*
E2	*Estradiol*
EDI	*Enhanced depth image*
ETDRS	*Early Treatment Diabetic Retinopathy Study*
FAZ	*Foveal Avascular Zone*
FSH	*Follicle-stimulating hormone*
GC	*Ganglion cell*
GCC	*Ganglion cell complex*
GCL	*Ganglion Cell layer*
GPER	*G protein-coupled estrogen receptor*
HDL	*High density lipoprotein*
IIH	*Idiopathic intracranial hypertension*
IL	*Interleukin*
IOP	*Intra ocular pressure*
IPL	*Inner plexiform layer*
LASIK	*laser -assisted in situ keratomileusis*
LC	*Lamina cribrosa*
LH	*luteinizing hormone*
MDA	*Malondialdehyde*
NADPH	*Nicotinamide adenine dinucleotide phosphate*

List of Abbreviations cont...

Abb.	Full term
NF-Kb	*Nuclear factor kappa-light-chain-enhancer of activated B cells*
NO	*Nitric oxide*
OCT	*Optical coherence tomography*
OCP	*Oral contraceptive pills*
ONH	*Optic nerve head*
PCA	*Posterior ciliary artery*
PCOS	*Polycystic ovary syndrome*
PDGF	*Platelet-derived growth factor*
PRK	*Photorefractive keratectomy*
Pt	*Prothrombin time*
RNFL	*Retinal nerve fiber layer*
ROS	*Reactive oxygen species*
RPE	*Retinal pigment epithelium*
SD-OCT	*Spectral domain optical coherence tomography*
SOD2	*Superoxide dismutase 2*
TD-OCT	*Time domain optical coherence tomography*
TLRS	*Toll like receptors*
TNF-α	*Tumor necrosis factor alpha*
VEGF	*Vascular endothelial growth factor*
α-SMA	*Alpha-smooth muscle actin*

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INTRODUCTION

Oral contraceptive pills (OCP) have some risks and side effects with regard to several organs, one of which is the eye. Estrogen & progesterone receptors have been shown to be present in various eye structures, such as the choroid, retina, conjunctiva, cornea, Meibomian glands, and lens [1].

Egypt Demographic and Health Survey (EDHS), 2005 provides that 57.5% of the married women in Egypt were using contraception. The most widely used methods are Intra Uterine Device (IUD), Oral contraceptive pill (OCP), and injection (respectively, 33.1%, 10.8% 7.7%) [2].

Over 100 million women around the world use hormonal contraceptive methods, whereas 93 million of them use combined oral contraceptive pills (COCs) [3].

The incidence of ocular side effects of oral contraception can be calculated as 1:230,000 in the United States, Canada, Australia, 1:180,000 in the German Federal Republic, and 1:14,000 in Great Britain [4].

Combined oral contraceptive pills (COCs) are widely indicted for contraception, menorrhagia, endometriosis, acne and hirsutism, fibroid uterus and premenstrual syndrome. The incidence of venous thromboembolic disease in healthy Female of reproductive age receiving COCs is increased from 4-5/10 000 women to 9-10/10 000. The anti-estrogenic activity of

progestins was estimated to be responsible for COCs-induced modifications of prothrombin time (PT), activated partial thromboplastin time (aPTT), fibrinogen, D-dimers as well as protein S, favoring a hypercoagulative state. Although the risk for venous thromboembolic disease is a three-fold higher in COCs users, compared to controls, it is eliminated along with the duration of use. Visual disturbances in women receiving COCs also seem to have cardiovascular background, being related to the expression of the progesterone receptors in ocular tissues [5].

Ocular complications or side effects reported in connection with oral contraceptives include dry eye symptoms, corneal disturbances, lens opacities, retinal vascular disorders, and proptosis, in addition, retinal edema, glaucoma, and hemorrhagic retinopathy have also been reported [6].

Severe neuro-ophthalmologic complications involve the 6th cranial nerve paralysis, parietal syndrome, hemianopsia, papillary edema and retrobulbar neuritis. Central retinal artery or vein occlusion, intraocular hemorrhages, aneurysms, macular or papillary edema and acute ischemic optic neuropathy represent the vascular complications of contraceptive pills [7].

Glaucoma is a serious condition that can develop from the use of oral contraceptives. The disease is characterized by damage to nerve tissue leading to a gradual loss of peripheral vision. It’s not entirely clear why contraceptive use would

possibly correlate to developing glaucoma, but optic nerve cells contain estrogen receptors that play a role in protecting the eyes from age-related decline. Research suggests that contraceptives could interfere in that process by lowering estrogen levels [8].

The biological actions of progestin are regulated by its receptors that belong in a superfamily of almost fifty ligand-activated nuclear transcription factors. This steroid receptor family includes the progestein, estrogen, androgen, glucocorticoid and mineralocorticoid receptors [9].

Sex hormones can affect the retina and choroid, so that OCP use could lead to result in alterations to OCT findings. Additionally, a correlation between sex hormones and disorders that may cause loss of vision has been described [10].

There could be a relationship between eyesight and estrogen, which have a protective effect on the eye. Therefore, it makes sense that the pills, which lowers a woman's total exposure to estrogen over a month, could affect her eyes. Birth control pills suppress cyclical spikes in women's estrogen levels, and over time, that dampening may contribute to retinal damage [11].

Estrogens seem to improve the symptoms of keratoconjunctivitis sicca and exhibit protective effect against glaucoma, cataractogenesis and degradation of corneal collagen. Moreover, the antioxidant and neuroprotective action of estrogens indicates their possible therapeutic use in neurodegenerative eye diseases, as well as AMD and diabetic retinopathy [12].