Correlation between Retinal Nerve Fibre Layer Thickness and Glycosylated Haemoglobin in Non Proliferative Diabetic Retinopathy

Thesis
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Content

List of Abbreviations

Abb.	Full term
ADA	American diabetes association
AGEs	Advanced glycosylation end-products
BCVA	Best corrected visual acuity
BRB	Blood retinal barrier
Ca2+	Calcium
CST	Cortistatin
CWS	Cotton wool spots
DAG-PKC	Diacylglycerol-proteinkinase C
DM	Diabetes mellitus
DME	Diabetic macular edema
DR	Diabetic retinopathy
Epo	Erythropoietin
ERG	Electroretinogram
ET-1	Endothelin-1
ETDRS	Early Treatment of Diabetic Retinopathy Study
GCC	Ganglion cell complex
GCL	Ganglion cell layer
GFAP	Glial acidic fibrilar protein
GLP-1	Glucagon-like peptide -1
HbA1c	Glycosylated haemoglobin
Hb-AGE	Hemoglobin advanced glycation end product
IL-1α	Interleukin 1α
IL-1β	Interleukin 1β
IOP	Intraocular pressure
IPL	Inner plexiform layer
IRBP	Interstitial retinol-binding protein
IRMA	Intraretinal microvascular abnormalities
M cell	Parasol ganglion cell
MCP-1	Monocyte chemotactic protein 1
mfERG	Multifocal electroretinogram
mfERG-IT	Multifocal electroretinogram implicit time
NMDA	N-methyl-D-aspartate
NO	Nitric oxide
NPDR	Non proliferative diabetic retinopathy
NVD	Neovascularization of the disc

List of Abbreviations Cont...

Abb.	Full term
NVE	Neovascularization elsewhere
OCT	Optical coherence tomography
p cell	Midget ganglparasol ganglion cell ()
PDR	Proliferative diabetic retinopathy
PEDF	Pigment epithelial-derived factor
RAGE	Receptor forAGEs
RAS	Renin–angiotensin system
RGC	Retinal ganglion cells
RNFL	Retinal nerve fibre layer
ROS	Reactive oxygen species
RPE	Retinal pigment epithelium
SQ	Spherical equivalent
SST	Somatostatin
STZ	Streptozotocin
TNF-α	Tumor necrosis factor-α
UHR	Ultrahigh-resolution
VEGF	Vascular endothelial growth factor

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INTRODUCTION

Diabetic retinopathy (DR) is one of the most common causes of visual loss in patients between thirty and sixty years old in the world. Although recent improvement, existing treatment with pharmacologic and laser treatment may not be enough in some people to prevent visual loss. DR is mostly a vascular disease, but recent studies have showed neurodegenerative changes even before the manifestation of micro vascular changes in patients with diabetes mellitus (DM**)** ***(Rodrigues et al., 2015)***.

Diabetes causes change in the electrophysiological measurements of retinal function and has an effect on the function of retinal neuronal cells before the blood–retinal barrier is extensively distorted ***(Carpineto et al., 2016)***.

In addition to ordinary pathogenesis of DR, impairments in visual evoked potentials, dark adaptation and contrast sensitivity have been noticed and show neuroretinal damage participation. Diabetes involves both retinal neurons and glial cells ***(Peng et al., 2009)***.

Retinal nerve fibre layer (RNFL) is a significant structural neuron in the retina layer is frequently shown to affect in the early pathogenesis of diabetic retinopathy. Some studies have detected RNFL defects in people with diabetes ***(Nor-Sharina et al., 2013).***

Optical coherence tomography(OCT) is non invasive examination helps the clinician to observe signs of neurodegenerative changes in the retina and detects neuroretinal changes in the early stages of DR and could be helpful in the development of a new management ***(Frydkjaer-Olsen et al., 2018).***

The glycosylated haemoglobin (HbA_{1c}) test has been recommended as screening test for Type 2 diabetes. HbA_{1c} levels represent a three months average of blood glucose concentration. It is a good predictors of the development of retinopathy ***(Bennett et al., 2007)***.

Consequently, the neuronal damages are irreversible and these damages are known to be induced by chronic glycemia. Whether, the neuro retinal changes are monitored in the early stage of DR, it will be better to correlate the neuro retinal changes with glycosylated haemoglobin level ***(Oshitari et al., 2014)***.

AIM OF THE WORK

The aim of our study is to determine correlation between retinal nerve fibre layer thickness measured by Optical coherence tomography and glycosylated haemoglobin in type 2 non proliferative diabetic retinopathy.

Chapter 1

DIABETIC RETINOPATHY

Diabetes mellitus is definited as a metabolic disease that characterized by a high blood sugar, either due to failure of pancreas to produce insulin, or due to insulin resistance ***(Gardner et al., 2011).***

DM is classified as Type 1 diabetes, which is an autoimmune disease may be due to infections or early childhood diet, and Type 2 diabetes, in which genetic defects in the cellular insulin receptor may give a reason for the insulin resistance ***(Yanoff and Sassani, 2014)***.

Diabetic retinopathy is the leading cause of blindness in patients with diabetes mellitus and refractory to treatments at the late stage of the diseses ***(Shi et al., 2017)***.

DR is the most common complication of diabetes and diabetes is expected to increase from 366 million in 2011 to 552 million in 2030, DR will become a serious problem in the future ***(Whiting et al., 2011)***.

DR is generally classified into non proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR).

Macular edema can be found in either group and does not used in the classification of level of retinopathy ***(Brownlee et al., 2016)***.

Pathophysiology:

Chronic hyperglycemia in poorly controlled diabetes decreases the production of endothelial and neuronal cell trophic factors, that causes edema, ischemia, hypoxia and neovascularization ***(Stewart, 2017)***.

The microvascular lesions in the early stages of diabetic retinopathy in humans and animals are characterized by the presence of capillary microaneurysms, loss of pericyte, and obliterated capillaries. Attraction and adhesion of white blood cells to the vascular wall, platelet aggregation and microthrombi are increased in the retinas of diabetic rats and humans. these changes are lead to apoptotic endothelial cells and ischemic changes ***(Kern and Huang, 2010)***.

There are metabolic pathways also stimulated by hyperglycaemia such as protein kinase C pathway, the polyol pathway influx and the hexosamine pathways, the synthesis of diacylglycerol-proteinkinase C (DAG-PKC), and the production of free radicals and advanced glycosylation end-products (AGEs) are critical in the progress of DR **(figure 1).** The activation of