Evaluation of the Relationship between Glycated Albumin and Peripheral Diabetic Neuropathy

Thesis

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in Endocrinology

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List of Abbreviations

Abb.	Full term
A1C or HbA1c	*Glycated hemoglobin*
ADA	*American Diabetes Association*
AGEs	*Advanced glycation end products*
ALA	*Alpha lipoic acid*
BCP	*Bromocresolpurple*
CAN	*Cardiovascular autonomic neuropathy*
CKD	*Chronic kidney disease*
CLD	*Chronic liver disease*
DC	*Direct current*
DM	*Diabetes mellitus*
DN	*Diabetic neuropathy*
DPN	*Diabetic peripheral neuropathy*
DPP	*Diabetes Prevention Program*
DSPN	*Distal symmetric polyneuropathy*
ED	*Erectile dysfunction*
ELBIA	*Enzyme-likedboronate immuneoassay*
ELISA	*Enzyme Linked Immunosorbent Assay*
ER	*Extended release*
FDA	*The Food and Drug Administration*
GA	*Glycated albumin*
GSH	*Glutathione*
GSSG	*Glutathione disulfide*
Hb	*Hemoglobin*
HDL	*High-density lipoprotein*
HPLC	*High performance liquid chromatography*
HRV	*Heart rate variability*
IFG	*Impaired fasting glucose*
IGT	*Impaired glucose tolerance*

List of Abbreviations (Cont...)

Abb.	Full term
KORA	*(Cooperative Research in the Region of Augsburg) study*
LDDP	*Length-dependent diabetic polyneuropathy*
NAD+	*Nicotinamide adenine dinucleotide*
NADPH	*Nicotinamide adenine dinucleotide phosphate*
Nav	*Voltage-gated sodium channels*
NBT	*Nitroblue tetrazolium*
NCS	*Nerve conduction studies*
NCV	*Nerve conduction velocity*
NGT	*Normal glucose tolerance*
NP	*Neuropathic pain*
OGTT	*Oral glucose tolerance test*
OS	*Oxidative stress*
PAGE electrophoresis	*Polyacrylamide gel electrophoresis*
PDN	*Proximal diabetic neuropathy*
PKC	*Protein kinase C*
RAGE	*Receptor for advanced glycation endproducts*
ROS	*Reactive oxygen species*
RPMA	*Right peroneal motor amplitude*
RPMCV	*Right peroneal motor velocity*
RPML	*Right peroneal motor latency*
RSSA	*Right sural sensory amplitude*
RSSCV	*Right sural sensory velocity*
RSSL	*Right sural sensory latency*
RTMA	*Right tibial motor amplitude*
RTMCV	*Right tibial motor velocity*
RTML	*Right tibial motor latency*
SNAP	*Sensory nerve action potential*

List of Abbreviations (Cont...)

Abb.	Full term
SNRI	*Serotonin norepinphrine reuptake*
SSRI	*Selective serotonin reuptake inhibitor*
SWME	*Semmes-Weinstein Monofilament Examination*
TCA	*Tricyclic antidepressant*
TTX-R	*Tetrodotoxin-Resistant*

INTRODUCTION

Diabetes: is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of different organs, especially the eyes, kidneys, nerves, heart, and blood vessels ***(American Diabetes Association, 2012)***.

Diabetes has become one of the largest global health-care problems of the 21 st century. The number of people with diabetes worldwide is predicted to double between 2000 and 2030, reaching a pandemic level of 366 million people ***(Hossain et al., 2007)***.

Diabetes causes a wide variety of acute, chronic, focal, and diffuse neuropathy syndromes. By far the most common is DPN, which accounts for 75% of diabetic neuropathy, Diabetic polyneuropathy (DPN), which has a lifetime prevalence of approximately 50%, is the most common diabetic complication; DPN is a leading cause for disability due to foot ulceration and amputation, gait disturbance, and fall-related injury. Approximately 20 to 30% of patients with DPN suffer from neuropathic pain, DPN significantly lowers quality of life and substantially increases health costs associated with diabetes ***(Tesfaye and Selvarajah, 2012)***.

Glycated albumin (GA): a ketoamine formed by non-enzymatic glycation of serum albumin, reflects short-term (2–3 weeks) mean glycemic levels ***(Furusyo and Hayashi, 2013).***

HbA1c, the result of the non enzymatic glycation of hemoglobin, reflects average glycemia over the preceding 8–12 weeks ***(Nathan et al., 2008)***.

The concentration of GA in serum, with a half-life of 12–19 days, would be an excellent index of recent glycemia. In addition to directly measuring the effects of hyperglycemia on the most prevalent plasma protein, GA has been directly implicated as a causal factor in several major complications of diabetes ***(Cohen and Clements, 1999).***

GA values are not affected by changes in erythrocyte lifespan ***(Koseck et al., 2005)***, and measurement of GA is not influenced by anemia or other conditions which invalidate HbA1c measurements in the diagnosis of diabetes ***(Furusyo et al., 2013).***

Aim of the Work

To evaluate the relationship between Glycated albumin and peripheral diabetic neuropathy.

Chapter 1
DIABETIC NEUROPATHY

Diabetic peripheral neuropathy (DPN) is a common complication estimated to affect 30-50% of individuals with diabetes ***(Deshpande et al., 2008).***

It is the most frequent and annoying complication of diabetes mellitus (DM), leading to the greatest morbidity and mortality and giving rise to a huge economic trouble for diabetes care, 2-3%develop a foot ulcer annually ***(Stockl et al., 2004).***

The neuropathies developing in patients with diabetes are known to be heterogenous by their symptoms, pattern of neurologic involvement, course, pathologic alterations, and underlying mechanisms ***(Dyck et al., 2005).***

A definition of peripheral neuropathic pain (NP) in diabetes is "pain arising as a direct consequence of abnormalities in the peripheral somatosensory system in people with diabetes" ***(Treede et al., 2008).***

This chapter will discuss:

- Pathophysiology of diabetic neuropathy.
- Risk factors of DN.
- Classification of DN.