PhD Thesis Summary

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"Effect of Glycemic Control on Soluble RAGE and Oxidative Stress in Type 2 Diabetic Patients"

The present study was designed to evaluate the effect of glycemic control on soluble receptor of advanced glycation end product (sRAGE) and some oxidative stress markers in type 2 diabetic patients.

This study was conducted in the Out-patient Clinic of Beni-Suef University Hospital between September 2011 and June 2012 and comprising 90 subjects who were subdivided into 20 healthy control volunteers and 70 patients with type 2 diabetes mellitus (T2DM).

All patients enrolled in the study fulfilled the following criteria: age between 35-70 years; receiving stable antidiabetic therapy (sulfonylurea, metformin, thiazoldinedione and/or insulin) for at least 6-8 months and no history of ketoacidosis. In hypertensive diabetic patients submitted to the study, the antihypertensive treatments were angiotensin converting enzyme inhibitors, angiotensin receptor blockers, Ca^{2+} channel blockers, β-blockers and/or diuretics for at least 6-8 months.

Exclusion criteria included the following: clinically significant hepatic, neurological, endocrinologic or other major systemic diseases, such as malignancy; elevated plasma transaminase activities over twice the upper limit of normal; elevated plasma creatinine concentrations (>150 μmol/L or 1.7 mg/dl); acute major cardiovascular events in the previous 6 months; acute illnesses; current evidence of acute or chronic inflammatory diseases and hormone replacement therapy for women subjected to the study. Exclusion criteria also included treatment with glucocorticoids, antineoplastic agents, psychoactive agents, bronchodilators, statins or vitamin supplements.

The patients enrolled in the present study were classified according to glycemic control [*good glycemic control* (glycated hemoglobin (HbA_{1c}) ≤ 7.0 %) and *poor glycemic control* (HbA_{1c} > 7.0 %)] with or without hypertension (SBP > 140 mmHg or DBP > 90 mmHg) along with normal subjects as follows:

I- Control healthy subjects [Group (1)]: It included twenty healthy individuals, age– and body mass index (BMI)–matched with diabetic patients.

II- Good controlled diabetics [Group (2)]: It was composed of twenty eight good controlled diabetics (GCD).

III- Poorly controlled diabetics [Group (3)]: It was composed of forty two poorly controlled diabetics (PCD).

Ten milliliters of venous blood samples were withdrawn after 12-14 hours overnight fast from each subject enrolled in the study. Each blood sample was collected into tubes containing EDTA and divided into 2 aliquots. The first aliquot was of 4 ml whole blood used for estimation of glutathione (GSH), HbA_{1c} and superoxide dismutase (SOD) activity. The second aliquot was of 6 ml blood centrifuged at 2000 x g for 10 minutes to obtain plasma for estimation of plasma glucose levels, alanine transaminase (ALT) and aspartate transaminase (AST) activities, plasma creatinine and lipid profile. The remaining plasma was stored at –20ºC for subsequent estimation of C-peptide, sRAGE, vascular cell adhesion molecule-1(VCAM-1), oxidized low density lipoprotein (ox-LDL) and total nitric oxide (NO_x) levels.

The present study showed a significant increase in fasting plasma glucose (FPG) levels in both diabetic groups compared with normal controls and increased HbA_{1c} levels in PCD compared with GCD. The increase in HbA_{1c} is attributable to the intracellular hyperglycemia which increases non-enzymatic attachment of glucose molecules to primary amino groups of hemoglobin protein, forming stable Amadori products