Plasma Levels of Nitric Oxide and Glycated Haemoglobin in Hausa/Fulani Type 2 Diabetic Patients with Erectile Dysfunction

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DOI: 10.36347/SJAMS.2019.v07i11.055 | Received: 06.11.2019 | Accepted: 20.11.2019 | Published: 28.11.2019

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Abstract

Nitric Oxide (NO) is a crucial player in vascular homeostasis. NO is synthesized within endothelial cells and its plasma levels decreases in patients with diabetic complications like erectile dysfunction. Diabetes mellitus, more in particular type 2, is a known causative factor of endothelial activation and resulting to endothelial injury and erectile dysfunction. This study was carried out to determine the plasma levels of nitric oxide and glycated haemoglobin in Hausa/Fulani type 2 diabetic patients with erectile dysfunction. The study was a cross sectional one carried out at Specialist Hospital, Sokoto from June to December 2018. The patients were assessed; the assessments include history (a questionnaire) and clinical examination. Nitric oxide and glycated haemoglobin were determined in forty (40) male type 2 diabetic subjects with erectile dysfunction and forty-five (45) male type 2 diabetic subjects with no erectile dysfunction using enzyme linked immunosorbent assay method. There were significant (p < 0.05) difference between the mean concentration of nitric oxide in type 2 diabetic subjects with erectile dysfunction (45.21 ± 3.77µmol/L) compared to type 2 diabetic subjects with no erectile dysfunction (69.59 ± 4.40µmol/L). There was significant (p < 0.05) difference between the mean concentration of glycated haemoglobin in type 2 diabetic subjects with erectile dysfunction (11.84±0.53%) compared to type 2 diabetic subjects with no erectile dysfunction (8.34±0.71%). This present study revealed that, plasma level of nitric oxide in type 2 diabetic patients with erectile dysfunction was significantly lower, while the level of glycated haemoglobin was significantly higher in Hausa/Fulani. These may serve as markers that could provide an adjuvant intervention for the prevention of chronic diabetic complications.

Keywords: Type 2 diabetes mellitus, Nitric Oxide, Glycated Haemoglobin, Hausa/Fulani.

INTRODUCTION

Nitric Oxide (NO) is a crucial player in vascular homeostasis. NO is synthesized within endothelial cells, during conversion of L-arginine to L-citrulline by endothelial nitric oxide synthase (eNOS) [1]. It is released from endothelial cells mainly in response to shear stress elicited by the circulating blood or receptor-operated substances such as acetylcholine, bradykinin, or serotonin. Its plasma levels decrease in patients with diabetic complications like erectile dysfunction due to prolong activation and injury to the endothelium [2]. NO diffuses to vascular smooth muscle cells (VSMC) and activates soluble guanylate cyclase (sGC), yielding increased levels of cyclic guanosine-3,5-monophosphatate (cGMP) and relaxation of VSMC. Additionally, NO also prevents leukocyte adhesion and migration, smooth muscle cell proliferation, platelet adhesion and aggregation, and opposes apoptosis and inflammation having an overall antiatherogenic effect[3]. The half-life of NO is very short (less than 4 s). It is rapidly metabolized to nitrite and then to nitrate before being excreted in the urine. Alternatively, NO can also be an endocrine vasoregulator, modulating blood flow in the microcirculation. Importantly, reduced eNOS expression and/or NO bioavailability is associated with endothelial dysfunction.

Type 2 diabetes mellitus (also known as non-insulin -dependent diabetes mellitus (NIDDM) refers to patients with diabetes mellitus characterized by insulin resistance or a state of relative insulin deficiency [4]. Clinical studies often use diabetes onset after age of 30 years as an operational criterion for type 2 diabetes mellitus [4]. Type 2 diabetes mellitus is insidious and may be present for years before being diagnosed [5]. Approximately, a good percentage of all diagnosed cases of diabetes mellitus is Type 2 and may be as many undiagnosed cases of Type 2 as diagnosed cases [5].
Glycated proteins are formed post-translationally, from the slow non-enzymatic reaction between glucose and amino groups on protein [7]. Measurement of glycated proteins primarily glycated haemoglobin is widely used for routine monitoring of long-term glucose status in patients with diabetes mellitus [8]. During normal ageing, glucose binds non-enzymatically to free amino groups in proteins and forms Amadori adducts through a series of oxidative and non-oxidative reactions [9]. Hyperglycaemia and oxidative stress probably confer Amadori adducts the opportunity to continue to rearrange and generate irreversible advanced glycation end products (AGEs) in diabetes [10]. The impact of AGES on retinal capillary cells is related to their capacity to accumulate in tissues over time. To form cross-links and to generate oxygen derived free radicals [10]. Additionally, binding of AGEs with their receptors may provoke sustained cell activation and further oxidative stress that could lead to endothelial injury and subsequently erectile dysfunction [8]. Glycated haemoglobin (GHb) also referred to as glycohaemoglobin, glycosylated haemoglobin (Hb A1c or HbA1) is a term used to describe a series of stable minor haemoglobin components formed slowly and non-enzymatically from haemoglobin and glucose [7]. The formation of glycated haemoglobin includes an intermediate shift base that is called "preA1c or labile A1c [11]. This material is formed rapidly with hyperglycaemia and interferes with some glycated haemoglobin assay methods, primarily those that are charged based [11]. The rate of synthesis of glycated haemoglobin is a function of the concentration of glucose to which the erythrocytes are exposed [8]. Hence glycated haemoglobin is a clinically useful index of mean glycemia during the preceding 120 days, the average life span of erythrocyte [12]. Glycated haemoglobin is also used as a measure of risk for the development of diabetes complications like erectile dysfunction [13].

**MATERIALS AND METHODS**

The research was carried out in the Department of Chemical Pathology and Immunology, College of Health Sciences (CHS) and Department of Medicine Specialist Hospital Sokoto. A total of 135 participants were consecutively selected for the study. Only diabetic, diabetic patients with erectile dysfunction and apparently healthy individuals who fulfilled the inclusion criteria and agreed to participate in the study were selected. Diabetic subjects were selected from diabetic clinics in the Department of Medicine Specialist Hospital, Sokoto. Preliminary information such as age, sex, height, weight of the patients, duration of the disease and medications were obtained using a questionnaire. The control subjects were 50 apparently healthy individuals. Those with history of liver diseases and cigarette smoking were excluded from the study. Type 2 diabetic patients and apparently healthy individuals aged 18 years to 60 years were recruited into the study. Type 1 diabetic patient, Hypertensive patient, Diabetic patient with coexisting other endocrine disorders, female and diabetic patient that consume alcohol were excluded from the study. Individuals who were non-diabetic and who have never had any family history of diabetes were included in the study as controls. Participants (Diabetics patients and apparently healthy controls) were fully informed, and their consent was obtained before the commencement of the research. Participants were allowed to withdraw from the study at any time and for any reason. Approval was obtained from the Ethics and Research Committee of the Specialist Hospital Sokoto. The study was a descriptive cross-sectional study, which was performed on Diabetic subjects attending Diabetic Clinic at Specialist Hospital Sokoto, for a period of 12 months. The diabetic patients were categorized into 2;

Group A1. Diabetic patient with erectile dysfunction (40)

Group A2. Diabetic patient with no erectile dysfunction (45)

Three milliliter (3ml) of whole blood was collected from each diabetic subjects and controls. The three milliliter (3ml) was placed in EDTA bottles for...
Nitric Oxide and glycated haemoglobin. The EDTA samples were stored at 2°C.

**STATISTICAL ANALYSIS**

The data obtained were analyzed using Microsoft Office Excel 2007 and SPSS software version 20.0 of 2016. The results of plasma fasting glucose and lipid profile obtained from diabetic subjects were compared with the controls using pair two-tailed student’s t-test for matched samples, while analysis of variance (ANOVA) was used to for comparisons of three (3) or more mean values of the parameters in the various groups. In each case where there was significant difference, a post-hoc analysis was carried out using Bonferroni multiple comparisons test. A p-value of less than or equal to 0.05 (P≤0.05) was considered as statistically significant.

**RESULTS**

A total of one hundred and thirty-five (135) male subjects participated in this study. Of this number, 40 were diabetic patients with erectile dysfunction, 45 were diabetic patients with no erectile dysfunction with their age ranged between 20 and 60 years and mean age and standard error of mean of (49.53±0.92) and (45.9 ± 1.48) respectively. The anthropometric data of the diabetic subjects were summarized in table 1, there were no significant (p>0.05) difference in the age, body weight, BMI and diastolic blood pressure of the diabetic subjects. However, the systolic blood pressure and height of the diabetic subjects was significantly higher than in group A2 (P<0.05).

**DISCUSSION**

Nitric Oxide (NO) plays vital role in vascular smooth muscle relaxation, which is a step in the process of penile erection. In this present study, the mean concentration of nitric oxide in type 2 diabetic subjects with erectile dysfunction was significantly lower compared to type 2 diabetic subjects without erectile dysfunction. This may be due to injury of the endothelial cell that produces NO [2]. Insulin resistance, as in the case of type 2 diabetes mellitus, may be another cause of the reduced nitric oxide production [6]. NO diffuses to vascular smooth muscle cells (VSMC) and activates soluble guanylate cyclase (sGC), yielding increased levels of cyclic guanosine-3′,5′-monophosphate (cGMP) and relaxation of VSMC. It is rapidly metabolized to nitrite and then to nitrate before being excreted in the urine. The fractional conversion of arginine to NO is also impaired and not normally enhanced by insulin. Alternatively, NO can also be an endocrine vaso-regulator, modulating blood flow in the microcirculation. Importantly, reduced eNOS expression and/or NO bioavailability is associated with endothelial dysfunction and erectile dysfunction in type 2 diabetes mellitus [14]. Nitric oxide is likely to be involved in the defective insulin mediated stimulation of blood flow in type 2 diabetes as well as in the pathogenesis of diabetic erectile dysfunction [15]. The diabetic subjects that participated in this study were currently on hypoglycaemic agents.
However, these drugs may affect nitric oxide synthase which may be another possible reason of reduced NO level in diabetic patient with erectile dysfunction. This correspond to a study carried by Tessari, Cecchet [6] which revealed that, nitric oxide synthesis is reduced in type 2 diabetic subjects.

Endothelial dysfunction is the hallmark of erectile dysfunction in diabetic subjects and might be through PKC activation, activation of the hexosamine and polyol pathways and formation of advanced glycation end product [16]. This was in agreement with research carried out by Malavige and Levy [17]. However, the plasma level of glycated haemoglobin in this present study was significantly high in type 2 diabetic subjects with erectile dysfunction compared to type 2 diabetic subject without erectile dysfunction. These could be as a result prolong exposure of glucose to haemoglobin that result to non-enzymatic interaction forming advance glycated end products [18]. The clinical complications associated with diabetes are most likely the consequences of hyperglycaemia through altered metabolism, non-enzymatic glycation of protein and advanced glycosylated end-products (AGEs) that accumulated in long-lived proteins such as vascular collagen and reduce the elasticity of vessel walls [19]. This correlate with a study carried out by Verma, Paneri [20] in Indian, which revealed that amount of carbohydrate attached to the HbA1c increases in patient diabetic complication. Also, in another study, it revealed that diabetic subjects with poorly controlled glucose showed a significant correlation between HbA1c and diabetic complications [21].

CONCLUSIONS

This present study revealed that, plasma level of nitric oxide in type 2 diabetic patients with erectile dysfunction was significantly lower, while the level of glycated haemoglobin was significantly higher in Hausa/Fulani. These may serve as markers that could provide an adjuvant intervention for the prevention of chronic diabetic complications.

REFERENCES