

Effect of glycemic control and hypertension on Serum basic amino acids in type II diabetes mellitus.

Ghassan A.AL- Shamma * PhD
AbdulRahman A.AL-Bazzaz*PhD
Faiz K.Asker*PhD
Mohammed Numan**PhD

Summary :

Background : Abnormal insulin secretion has been considered the main cause of changes in carbohydrate ,lipid and protein metabolism in diabetes mellitus(DM) with increased muscle proteolysis and amino acid mobilization.

Aim : to study the effect of glycemic control and hypertension, on three basic amino acids ,arginine (Arg.) ,lysine (Lys) & histidine (His) in type II DM.

Subjects: Fifty five patients with type II diabetes mellitus (DM) were included in the study .They were 39 normotensive & 16 hypertensives with different grades of glycemic control as revealed by the level of glycated Hb. (HbA_{1c}). Thirty eight were with poor control ; HbA_{1c} > 8.5 % , (27 normotensives & 11 hypertensives) while 17 were with acceptable range of control, HbA_{1c} 6.8 - 8.5 % (12 normotensives & 5 hypertensives).

Forty non diabetic subjects (28 normotensives & 12 hypertensives) were also included in the study as a control group.

Methods: Glycated Hb (HbA_{1c}) was measured by affinity resin column chromatography and serum amino acid analysis was done by reversed high performance liquid chromatography.

The results show that type II DM had caused a significant reduction in serum Arg (a precursor of nitric oxide which has an important role in the reduction of diabetic complications) with a significant elevation in serum Lys ,while no change in serum His could be seen. Hypertension , on the other hand , has caused a significant elevation in serum His in both diabetics & non diabetics. Serum Arg was not changed while a significant elevation in serum Lys. was found in the non diabetic hypertensive subjects ,which disappeared in the diabetic hypertensive patients. No effect of the glycemic control on the concentration of any of the three amino acids could be detected in the diabetics of the present study.

The possible suggestions and explanations for these events are mentioned.

Key words: basic amino acids , diabetes mellitus , hypertension , glycemic control

J Fac Med Baghdad
2005; Vol. 47, No.3
Received Feb. 2003
Accepted July 2005

Introduction

Abnormal insulin secretion or action has been considered the main cause of changes in carbohydrate ,lipid & protein metabolism in diabetes mellitus (1 ,2) , and insulin deficiency was reported to accompany augmented proteolysis in muscles with increased amino acid mobilization (3). Accordingly the degree of glycemic control is an important factor in modulating the general action of diabetes mellitus. On the other hand insulin resistance syndrome was reported to associate elevated blood pressure (4 ,5) .This could be mediated through the increase in catecholamines in both diabetic and non diabetic people (6) .

The present work was undertaken to study the effect of type II D M on three basic amino acids arginine (Arg), lysine (Lys) & histidine (His) & some modulating factors namely the glycemic control & hypertension.

Material & Methods :

A. Subjects:

1. Diabetic patients :

Fifty five patients with type II DM attending the diabetic clinic of the university Hospital of Saddam College of Medicine were included in this study They were of different degrees of glycemic control . Some were normotensives & others were hypertensives .

2. Forty non diabetic normotensive & hypertensive people of matching age and sex were included in the study for comparison.

B. Blood samples and laboratory methods:

Ten ml of venous blood were aspirated after 12 hour fast from each patient and control subject. An aliquot of 2 ml. were put in ethylene diamine tetra acetic acid (EDTA) tubes for measurement of glycated Hb (HbA_{1c}) & PCV, kept at 4 C until the time of assay (within 1 -3 days). HbA_{1c} was measured by affinity resin column chromatography using kits supplied by Sigma Diagnostics.

Another aliquot of the blood was put in a plain tube

* Departments of chemistry & Biochemistry ,AL-Nahrean college of Medicine ,Baghdad , Iraq.

** Departments of Medicine ,AL-Nahrean college of Medicine ,Baghdad , Iraq.

and allowed to clot. Serum was separated after centrifugation and stored at -70 C. pending amino acid analysis which was done by reversed phase high performance liquid chromatography after pre-column derivatization following the method of Bird 1989 (7) with some modifications.

Results:

Analysis of the data obtained from the subjects included in this study revealed the following:

a. thirty eight of the diabetics were poorly controlled with HbA1c level more than 8.5 % (27 normotensives & 11 hypertensives).

b. Seventeen diabetics had acceptable range of glycemic control with HbA1c between 6.8 - 8.5 % (12 normotensives, & 5 hypertensives).

c. Among the 40 non diabetics 28 were normotensives and 12 were hypertensives.

Table (1) shows the concentrations of the three amino acids measured in this study, arginine, lysine and histidine. There is a significant reduction in the concentration of serum arginine & lysine in the normotensives of both groups of diabetic patients as compared to the non diabetic normotensive people. No significant difference could be seen between the normotensive and hypertensive diabetics.

However serum lys. Was significantly higher in the hypertensives than the normotensives of the non diabetic group. serum his, on the other hand, was markedly affected by hypertension in both diabetic & non diabetic groups, being higher in the hypertensives.

Table (1) showing the concentrations of the basic amino acids in the diabetic and the non diabetic normo- & hypertensive people

	Arginine	Lysine	Histidine
A Diabetics			
1. poor control			
normotensives (27)	90.53* ± 24.3	291.0* ± 56.3	80.9 ± 20.8
hypertensives (11)	90.1 ± 25.0	291.0 ± 72.9	164.2* ± 38.0
2. acceptable control			
normotensive (12)	81.2* ± 18.9	294.8* ± 58.3	91.1 ± 20.4
hypertensives (5)	95.6 ± 17.1	241.9 ± 41.2	165.0* ± 15.9
B Non diabetics			
normotensives (28)	120.2 ± 37.8	237.4 ± 56.0	81.4 ± 23.6
hypertensives (12)	143.8 ± 26.9	299.0* ± 54.5	153.2* ± 28.8

* values are significantly different from the non diabetics.

(*) values between normotensives & hypertensives of the same group are significantly different

- All values are expressed as $\mu\text{mol/L}$.

- poor control HbA1c > 8.5, acceptable control HbA1c 6.8 - 8.5.

Discussion:

Plasma arginine, which is a part of the urea cycle,

was reported to decrease in diabetic patients (1). This is most likely due to increased arginase activity in the liver of diabetics (8). Reduction in serum arginine associates the reduction in insulin secretion, and infusion of arginine to patients with early onset type II diabetes mellitus had resulted in an increase in insulin secretion to the same extent as glucose and glucagon (9). It may also increase the concentration of interleukin-1 alpha which would result in a reduction in advanced stage non enzymatic glycosylation products, (10). The reduction in arginine was also suggested to cause a reduction in the release of endothelium derived nitric oxide through a decrease in the vascular Na - K ATPase activity and this consequently leads to impairment of vascular relaxation usually seen in hyperglycemia and DM (11).

However advanced end products of glycation & glycooxidation (N-carboxy-methyl lysine) are significantly increased in patients with type II DM (12).

Increased lysine in type II DM was attributed to decreased peripheral insulin action & increased muscle proteolysis (2).

The incidence of insulin resistance in hypertension was reported to be about 29 % and increased to more than 80 % in combination with glucose intolerance and dyslipidemia (13,14).

The cause of increased serum histidine in hypertension is not available at the time being. The possible relation to an alteration in the activity of histidase enzyme activity could be considered for a future work in this field.

References:

1. Foss MC, Viachokosta FV, & Aoki-TT (1989), Carbohydrate Lipid and amino acid metabolism of insulin dependent diabetic patients regulated by an artificial B-cell unit Diabetes Res. 11:1-8.
2. Rosenlund -BL (1993), Effect of insulin on free amino acids in plasma and the role of amino acid metabolism in the etiology of diabetic micro-angiopathy. ; Biochem Med. Metab. Biol. 49:375-391.
3. Hagenfeldt -L, Dhiquist -G & Presson-B (1989); Plasma amino acid in relation to metabolic control in insulin dependent children, Acta Paediatr. Scand. 78: 278-282.
4. Donahue -RP, Bean-JA, Decarlo-Donahue-AR & Goldberg -RB (1997)-Independent effects of insulin resistance and insulin level in the insulin resistant syndrome: Evidence from the Miami community Health Study: Diabetes 46 (suppl. 1) 136-A (abstract 0526).
5. Sato -T, Nara -Y, Kato-Y & Yamori -Y (1996); effect of antihypertensive treatment with alicepiril on insulin resistance in diabetic spontaneously hypertensive rats, Metabolism 45:457-462.
6. Vannini-P, Marchesini -G, Fortani -G, Angiolini -A, Ciavarella-A, Zoli -M, & Pisi - (1982), Branched chain amino acids and alanine indices of the metabolic control type I (insulin dependent) & type II (non-insulin dependent) diabetic patients. Diabetologia 22 : 217 - 219.
7. Bird -JM, (1989) High performance liquid chromatography. Principles & clinic applications, BMJ 299 : 783 - 787.

8. Spolarics -Z & Bond- JS (1989), Comparison of biochemical properties of liver argina: from streptozotocin - induced diabetic and control mice , Arch. Biochem. Biophys. 274 426 -433.
9. Cheng -HM , Jap -TS , Le c - KT, Kivok - CF ,et. al. (1992) .Arginine induced insu release in patients with newly onset non insulin dependent diabetes mellitus , Cher Taipei 50: 184-188.
10. Hayde -M .Vierhapper -H , Lubec -B, Popow -C , Weniger -M , Xi -Z & Lubec - (1994). Low dose dietary L-arginine increases plasma interleukin -I- alpa but r interlukin -I - beta in patients with diabetes mellitus. Cytokins , 6 : " 79 — 82.
11. Cupta - S , Sassman -A, MacArther -CS, Torheim ~K , et. al.(1992) Endothelii dependent inhibition of Na-K ATPase activity in rabbit aorta by hyperglycemia .Possil role of endothelium -derived nitric oxide , J .Clin. Invest. 90: 727 - 732.
12. Kilhoved -BK , Berg- TJ, Birkdamd -Kl.Jhorshy -P & Hensen-KF (1999) Serum levels of advanced glycation end products are increased in type 2 diabetes and coronary heart disease , Diabetes care , 22 :1543 - 1548.
13. Bonora -E , Kiechi-S , Willeit -J , oborhollenzer -F, Egger -G & Muggeo -M (1997). Prevelance of insulin resistance in metabolic disease from a population - based study ., Diabetes , 46 (suppl.1); 136 A (Abstract 0525)
14. Wei-M , Haffer -S , & Stem -M (1997) High fasting glucose as a predictor of total and cardiovascular disease (CVD) mortality in patients with NIDDM., Diabetes , 46 (suppl.1) : 137 A (Abstract 0529).