ORIGINAL RESEARCH PAPER

Medical Science

STUDY OF SERUM AMYLIN IN TYPE-2 DIABETES MELLITUS PATIENTS.

KEY WORDS: Type-2 DM, serum amylin, IAPP.

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ABSTRACT

Background- Type 2 diabetes is a worldwide pandemic that will continue to grow and, through increased insulin resistance and decreased insulin uptake, high blood glucose or hyperglycemia, is increasingly hard to combat. Amylin, which is synthesized in beta cells of the pancreas from its precursor proamylin and plays an important role in early intracellular amyloid formation as well. It has been seen in type 2 diabetics that this polypeptide undergoes a transformation into a mature fibrillar state, causing amyloid depositions intracellularly in the beta cells.

Material & methods- The study was conducted on 80 subjects with Type 2 diabetes mellitus(Group I) & 80 healthy controls(Group II). Biochemical tests done were Serum glucose(measured by Glucose oxidase – peroxidase end point assay), serum Amylin(measured by ELISA). Data was analysed by SPSS Software and p-value<0.05 was considered significant.

Results- The mean serum Amylin in type-2 diabetic patients were (9.2± 2.5) & in controls were (4.5± 0.5) respectively. These were found to be statistically highly significant($p<0.001$).

Conclusion- The present study depicts that Type 2 diabetic subjects have significantly higher serum amylin levels as compared to healthy controls.

INTRODUCTION-

Type 2 Diabetes mellitus is a heterogeneous syndrome characterized by abnormalities in carbohydrate and fat metabolism. The causes of Type 2 Diabetes are multi-factorial and include both genetic and environmental elements that affect beta-cell function and tissue (muscle, liver, adipose tissue, and pancreas) insulin sensitivity. Although there is considerable debate as to the relative contributions of beta-cell dysfunction and reduced insulin sensitivity to the pathogenesis of diabetes, it is generally agreed that both these factors play important roles.

Amylin or Islet Amyloid Polypeptide (IAPP) is a 37 residue polypeptide hormone that is secreted in conjunction with insulin from the pancreatic beta-cells in a 100:1 ratio [1]. IAPP is expressed on gene 12 by one single gene copy on the short arm of the chromosome [2]. In type 2 diabetes amylin misfolds and causes fibril formation. Usually, amyloid fibrils are formed by soluble proteins, which assemble to form insoluble fibers that are resistant to degradation.

In a healthy individual, amylin is co-secreted with insulin from the beta cells and is then excreted via the kidneys. The occurrence of islet amyloid fibril formation is less than 15% in non-diabetic patients, but is present in over 90% of diabetic subjects [3]. Amyloid is only seen in type 2 diabetics, because, in type 1 diabetics, the IAPP source is removed due to the destruction of the beta cells. Because insulin and IAPP are co-secreted, an increased level of human Islet Amyloid Polypeptide (hIAPP) which occurs in a state of insulin resistance, where insulin secretion increases to compensate can initiate the fibril formation. When IAPP is stored in the secretory granules of the beta-cells at about one to four millimolar concentration, which is about a thousand times the amount that is necessary to form amyloid fibrils.

One of the most widely investigated hypothesis that approaches the connection between type 2 diabetes and IAPP suggests that the damage caused by its interaction with the cell's membranes. With the human islets it was found that the alpha cells remained intact, while the beta cells decreased in number and amyloid fibrils were found densely packed intracellularly with their plasma IAPP levels being increased more than five times that of the baseline value. The results of such studies of transplanting the pancreatic islet cells proved a firm connection between amyloid fibrils and the destruction of beta cells that can lead to type 2 diabetes.

MATERIALS & METHODS-

The present study has been conducted on Type 2 Diabetic subjects of either gender and age attending the OPD of Department of Medicine, Tripura Medical college & Dr. B.R.A.M Teaching hospital from January 2021 to December 2021. The subjects were considered as Type 2 DM based on the American Diabetes Association guidelines (ADA) 2017.

The study was conducted on 160 subjects which was divided into two groups- 1) Group I- 80 subjects with Type 2 diabetes mellitus 2) Group II- 80 subjects of same age group of either sex were selected as controls.

An informed written consent was obtained from all the subjects and a detailed anthropometric parameters like height, weight and BMI was recorded. Exclusion criteria was regular alcohol or drug consumption, history of any metabolic disorder, renal disease, cerebrovascular or cardiovascular diseases, current treatment with any drug that alters glucose tolerance, any acute illness. On a prescheduled morning, the subjects were requested to arrive after overnight fast (at least 10 hour) to provide a fasting blood sample. After collecting fasting blood samples, the subjects were given 75g of glucose dissolved in 250ml of water. The blood was taken via venepuncture 2 hours after glucose load. After 30 minutes of collection, the blood sample was centrifuged for 10-15 minutes at 3000 rpm to obtain the serum and used for estimation of serum glucose(measured by Glucose oxidase – peroxidase end point assay), serum Amylin(measured by Enzyme Linked Immunosorbent Assay (ELISA). Data was analysed by SPSS Software and p-value<0.05 was considered significant.

RESULTS-

Basic anthropometric parameters of all subjects in Type 2 diabetic and healthy controls are summarized in table-1.

Table 1:Anthropometric parameters of Type 2 diabetic subjects and healthy subjects (controls)

Parameters	GROUP-I Type 2 diabetic subjects Mean ± SD (n=160)	GROUP-II Healthy subjects (controls) Mean ± SD (n=160)
AGE (yrs)	38± 6.0	40 ± 2.5
WEIGHT (kg)	60 ± 2.6	52 ± 4.2

HEIGHT (cm)	155 ± 6.0	159 ± 10
BMI (kg/m^2)	23.8 ± 2.5	19.6 ± 2.1

Table 2:biochemical Parameters Of Type 2 Diabetic Subjects And Healthy Subjects (control)

Parameters	GROUP-I Type 2 diabetic subjects Mean ± SD (n=160)	GROUP-II Healthy subjects (controls) Mean ± SD (n=160)
Fasting Plasma Glucose (mg/dl)	178.8 ± 36.5	76.0 ± 6.6
2-hour Plasma Glucose (mg/dl)	189.0 ± 42.3	92.0 ± 7.8
S. Amylin (pmol/l)	9.2± 2.5	4.5± 0.5

Table-2 shows, the biochemical parameters viz, plasma glucose(mg/dl), serum amylin (pmol/l) in Type 2 diabetic & healthy controls. The mean fasting plasma glucose level in mean ± SD were found to be significantly high in group-I (178.8 ± 36.5) as compared to group-II (76.0 ± 6.6 mg/dl; p< 0.0001)

The mean serum amylin levels in pmol/l mean ± SD were significantly higher in group-I (9.2 ± 2.5 pmol/l)as compared to group-II (4.5± 0.5) (p< 0.0001). The present study depicts that Type 2 diabetic subjects have significantly higher serum amylin levels as compared to healthy controls. (Table 3)

Table 3 Comparison Of Serum Amylin Levels Of Type 2 Diabetic Subjects And Healthy Subjects (controls)

Parameters	GROUP-I Type 2 diabetic subjects Mean ± SD (n=160)	GROUP-II Healthy subjects (controls) Mean ± SD (n=160)	'p' Value*
S. Amylin(pmol/l)	9.2 ± 2.5	4.5 ± 0.5	<0.0001

*p – value <0.0001 Highly Significant (HS)
p – value<0.01 Significant (S)
p – value>0.05 Non significant (NS)

DISCUSSION-

Type 2 diabetes is a worldwide pandemic that will continue to grow and, through increased insulin resistance and decreased insulin uptake, high blood glucose or hyperglycemia, is increasingly hard to combat. Amylin, which is considered the primary culprit for beta cell loss in T2DM patients, is synthesized in beta cells of the pancreas from its precursor proamylin and plays an important role in early intracellular amyloid formation as well. Islet beta-cell dysfunction was associated with deposited amylin and proamylin in beta cells in the form of islet amyloid. It has been seen in type 2 diabetics that this polypeptide undergoes a transformation into a mature fibrillar state, causing amyloid depositions intracellularly in the beta cells. It has now been determined that the mature state of the amyloid fibrils is not the cause of cell toxicity in the case of type 2 diabetes, but rather its oligomeric intermediates cause the cytotoxicity to occur at the beta cells. These oligomeric intermediates of amyloid fibrils have not yet been determined to have one specific mechanism of action for causing the cytotoxicity, but several theories of cell toxicity have been proposed including beta cell membrane disruption, endoplasmic reticulum stress, and oxygen radical formation. There is also a large possibility that a combination of such cytotoxic events caused by the aggregation of amyloid fibrils is what causes the damage to beta cells. The mechanism of cell toxicity due to hiAPP fibril deposition is one of the biggest questions left to answer.

The findings are in agreement with Nishimura s et al. (1991), who found that amylin concentrations were significantly higher in type 2 diabetic group than the Normal Glucose Tolerance group, suggesting a possible association between circulating amylin concentration and glucose tolerance.

CONCLUSION-

In the present study Type 2 diabetic patients serum amylin levels were found to be higher with comparison to healthy controls. Physiological functions of beta cells have major roles in different metabolic processes and tissues. The extent of amyloid deposition was associated with both loss of beta-cell mass and impairment in insulin secretion and glucose metabolism, suggesting a causative role of islet amyloid in the islet lesion of type 2 diabetes. Production of amyloid fibrils increases explosively after a certain level of nucleation is reached, causing increased beta cell death, the level of obesity and unhealthy living has resulted in an explosion in the number of individuals affected by type 2 diabetes. In much the same way that amylin agonists or peptide inhibitors can prevent the molecular explosion of fibrils, continuing research at this molecular level can provide a preventative medicine approach to the disease.

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