STUDY OF PLASMA INSULIN AND GLUCOSE PROFILE IN OBESE AND NON-OBESE NORMAL CONTROLS AND DIABETIC SUBJECTS

Pages with reference to book, From 39 To 42

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Abstract

Glucose tolerance test (GTT) with simultaneous estimation of immunoreactive insulin (IRI) were done in 108 subjects. The study groups comprised of non-obese and obese normal controls, obese subjects with chemical diabetes and subjects with clinical diabetes. Normal subjects showed relatively low fasting IRI level with a rapid IRI peak at one hour. The fasting IRI activity was three times higher in obese controls and diabetic subjects. In diabetics insulin secretion fell far short of the required level in the presence of rising glucose level. It is presumed that as in Western countries diabetic-syndrome in Pakistan also is a combination of poor insulin secretary rate and insulin resistance (JPMA 31:39, 1981).

Introduction

Classical diabetes mellitus as seen in west is a genetically determined disorder. There are two main clinical types i.e., juvenile (Type 1) and maturity onset (Type 2). However, in tropical countries certain variations have been encountered namely the 'J' type seen in Jamaica in young and thin insulin resistant patients (Hugh-Jones, 1955) and K type in Ugand awhich is associated with the episode of hypoglycemia (Shaper, 1964). Ibrahim (1962) in a study from East Pakistan (now Bangladesh) described yet another type of diabetes seen in underweight subjects of widely varying ages who showed a good response to oral hypoglycemic agents. He called it "tropical diabetes" and indicated the possibility of hepatic dysfunction in its aetiology. Wicks and Jones (1974) have emphasized the role of secondary factors such as pancreatic and hepatic disease in the genesis of diabetes in Rhodesia.

Our experience with maturity onset diabetes shows that nearly 50% of them are overweight and respond to diet and oral hypoglycemic agents. A small group of patients shows a relative insulin insensitivity without a tendency to ketosis. No relationship has been observed between diabetes and liver dysfunction (Haider et al., 1975).

Data on the insulin dynamics is scarce in Pakistan. Khalid et al (1974) showed a higher fasting insulin level in both obese and non-obese diabetic patients in Karachi. The results of immuno reactive assay of insulin (IRI) done in obese and non-obese controls and patients with diabetes are presented here.

Material and Methods

Included in this study were 108 subjects (30 males and 78 females). The patients were selected from the Diabetic clinic of PMRC Research Centre, Sir Ganga Ram Hospital, and the controls from the students and staff of Post-graduate Medical Institute and Medical Research Centre, F.J. Medical College, Lahore and subjects with normal GTT from the Diabetic Clinic.

The subjects were grouped according to the weight and the results of glucose tolerance test as follows:

(1) Normal GTT

(a) Non-obese (30)

(i) Young (20): 12 males and 8 females.
(ii) Middle age (10): one male and 9 females.
(b) Obese (20)
(i) Normal GTT (14): 3 males and 11 females.
(ii) Abnormal GTT (Chemical diabetes) 6 males.
(2) Diabetics:
(a) Non-obese (43)
(i) Newly diagnosed (20): 4 males and 16 females.
(ii) Known diabetics (off treatment) (23): 3 males and 20 females.
(b) Obese diabetics (15): one male and 14 females.

Persons weighing more than 20% above the ideal weight as per charts of Metropolitan Life Insurance Company, U.S.A., were classified as obese. All normal non-obese controls had a fasting blood glucose level of <105 mg% and 2 hours post-parandial glucose level were less than 120 mg/100 ml. In obese normal subjects the fasting glucose level was <105 mg/100 ml and 2 hours post-parandial levels were <30 mg/100 ml.

Six cases with chemical diabetes had a fasting blood glucose level > 110 mg/100 ml. Of 58 diabetics, 43 were non-obese and 15 obese. Their fasting blood glucose level ranged from 130-350 mg% and none had ketosis.

Glucose tolerance tests were carried out on patients who were fasting overnight (10-14 hours) with oral administration of 50 gm of glucose in 250 ml water. Venous blood samples were collected at 0,60,120 minutes in all cases for estimation of blood glucose and plasma insulin activity (IRI). Plasma glucose estimation was carried out by colorimetric method described by King and Wooten (1964). Plasma immuno-reactivc insulin (IRI) was determined by radio immunoassay method of Hales and Randle (1963). The insulin kits were obtained from the Radio Chemical Centre, Emersham, England.

Results

Table I: Age & Sex Distribution of Subjects, and Mean IR1 Values During GTT in Control, Obese and Diabetic Subjects. Number of Subject is shown in Parenthesis.

Subjects		*Age group in years*	*Sex*		*Mean IRI μU/ml*	*± S.D.*	
			Male	*Female*	*Fasting*	*one hour*	*two hours*
Control: (a) Normal weight							
(i) Young	(20)	17—30	12	8	11.85 ± 2.25	60.45 ± 7.85	44.45 ± 7.71
(ii) Middle aged	(10)	31—70	1	9	15.7 ± 2.85	76.27 ± 10.42	56.46 ± 6.89
(b) Obese							
(i) Normal GTT	(14)	30—75	3	11	37.1 ± 6.6	104.1 ± 9.8	86.2 ± 12.3
(ii) Abnormal GTT (chemical diabetes)	(6)	30—75	6	—	39.1 ± 6.8	84. 5 ± 6.03	160.0 ± 20.3
Diabetes: (a) Non-obese							
(i) Early diagnosed	(20)	25—42	4	16	29.5 ± 3.6	69.4 ± 8.2	56.4 ± 6.8
(ii) Known diabetic	(23)	43—65	3	20	40.3 ± 5.3	77.4 ± 12.2	61.6 ± 13.1
(b) Obese diabetics	(15)	30—60	1	14	31.8 ± 4.2	92.3 ± 11.3	83.7 ± 14

Table 1 shows the age and sex distribution of the subjects and their mean IRI values during the GTT. The mean fasting IRI values in non-obese controls (Young and middle age groups) ranged from 11.85

µµ/ml to 15.7 µµ/ml. The values are lower than those obtained in obese controls and the diabetic groups. The peak IRI response was achieved within one hour in non-obese controls. In obese normal subject, the mean fasting IRI values were higher i.e., 37.1 µµ/lm\ and comparable to the diabetic subjects.

Normal obese individuals showed an exaggerated insulin response with a peak within one hour. Six patients with chemical diabetes had a high mean fasting IRI value i.e. 39.1 µµ/ml but the peak insulin response was delayed and occurred at 2 hours after the glucose stimulus. In the group of diabetic patients both obese and non-obese, the fasting IRI was higher than in the control group but the subsequent insulin response even in obese diabetics was relatively less as compared to other groups.

Table II: Mean Blood Glucose and IRI Values During GTT in Diabetic Patients with Different Grades of Severity and Normal Controls.

The values are mean±S.E. The range of value is shown in Parenthesis.

Fasting glucose mg/100 ml	*No. of patients*	*% of total No. of cases*	*Tolerance test plasma glucose mg/100 ml*			*Mean IRI with GTT*		
			Fasting	*1 hour*	*2 hour*	*0min*	*60 min*	*120 min*
<100	5	13	89.8 ±3.4 (80-100)	201.6 ±19.8 (140-245)	156.4 ±11.3 (123-190)	33.3 ± 5.8	106.5 ±41.76	76.8 ± 9.7
101-125	4	9.7	118.7 ±3.1 (110-125)	199.5 ± 6.5 (183-215)	153. ± 5.8 (105-215)	30.03± 3.5	90.1 ±13.8	70.4 ±17.1
126-180	25	58.1	147.3 ±2.6 (130-175)	247.3 ± 8.5 (190-355)	238.5 ± 9.4 (150-320)	29.9 ± 2.9	76.8 ± 9.7	64.1 ±10.8
> 180	9	21.9	231.1 ±9.6 (190-245)	311.4 ±17.7 (236-400)	329.8 ±19.1 (230-415)	30.7 ± 6.9	69.3 ±12.6	50.9 ±12.5
Non-diabetic Control	20	—	71.7 ±3.04 (50-105)	109.2 ± 5.9 (84-144)	84.1 ± 5.1 (50-123)	11.85± 2.2	60.4 ± 7.8	44.4 ± 7.7

Table II shows the mean glucose and IRI values during the GTT in diabetic patients with different grades of severity, as judged by the fasting glucose values. These values are compared with 20 non-diabetic controls. The mean fasting IRI was nearly 3 times more and IRI values at 60 to 120 minutes were relatively less in relation to the blood glucose levels in diabetics of all grades of severity.

This blunted insulin response with rising blood glucose level was more marked in those with relatively more severe diabetes (fasting blood sugar > 180 mg%).

Table III: Relationship of Serum IRI to Serum Glucose Values in Normal Weight and Obese Controls and Diabetic Subjects (No. of Subjects Shown in Parenthesis).

Obese or non-obese	*Normal or diabetic*	*Serum IRI µµ/ml*			*Glucose mg/100 ml*		
		Fasting	*One hour*	*Two hour*	*Fasting*	*One hour*	*Two hour*
(I) Non-obese Group	(i) Normal (20)	11.85± 2.25	60.45± 7.85	44.45± 7.71	71.77± 3.04	109.27± 5.90	84.10± 5.17
	(ii) Diabetics (43)	34.28± 4.13	66.80±11.92	72.97±10.54	139.55± 9.72	245.40±10.99	235.75±17.51
(II) Obese Group	(*a*) Normal GTT (14)	37.10± 6.63	104.10± 9.88	86.25±12.31	86.3 ± 3.6	139.9 ± 6.48	116.2 ± 8.3
	(*b*) Abnormal GTT (Chemical (Diabetics (6)	39.1 ± 6.8	84.5 ± 6.03	160. ±20.3	116 ± 3.1	185 ± 5.8	160 ± 5.2
(III) Obese	Diabetics (155)	31.83± 4.25	92.31±11.34	83.79±14.68	167.8 ±13.4	254.5 ±16.5	238.2 ±20.7

Table III shows the relationship of serum IRI and blood glucose in obese and non-obese controls and the diabetic patients.

In non-obese group, the normal controls bad a mean IRI value of 11.85 µµ/ml compared to a much higher value in the diabetics i.e., 34.28 µµ/ml. The subsequent insulin response in this group of diabetics was relatively lower when simultaneously obtained mean blood glucose values are

considered.
In the obese group, normal controls had a high fasting IRI values i.e., 37.10 µµ/ml and showed a higher secretory rate of insulin at 1 hour i.e., 104.10 µµ/ml. A high insulin secretory rate was also noted in obese patients with chemical diabetes, but the response was delayed. In 15 obese diabetics, the mean fasting IRI value was 31.83 µµ/ml, which was comparable to that in obese non-diabetics. However, the subsequent IRI values were lower than in obese controls when compared with high blood glucose values at 1 hour and 2 hours (254.5 and 238.2 mg%).

Discussion

The clinical spectrum of diabetes varies in different geographical regions. Liver diseases (Ibrahim, 1962) and pancreatic insufficiency have been incriminated for some unusual features of diabetes in tropical region but the role of insulin resistance and deficiency has not been clearly defined. Khalid et al (1974) reported a significantly higher level of fasting plasma IRI in both obese and diabetic subjects as compared to normal controls. In their study role of insulin resistance rather than insulin deficiency was emphasised. In the present study insulin level were measured in fasting state and throughout the duration of GTT. The fasting IRI was much lower in normal non-obese, normal obese and diabetic subjects. The peak insulin secretion was reached within one hour in normal subjects. The obese normal subjects showed a high fasting IRI level with high secretory rate of insulin during the GTT, but the peak response was within one hour as in non-obese normal individuals. The obese patients with an abnormal GTT (chemical diabetes) had a high insulin secretory rate but with a delayed peak of insulin. In diabetics with various grade of severity, the fasting insulin levels were higher than those in normal non-obese individuals as has previously been observed by Khalid et al (1974). The insulin secretory response in the later stage of GTT fell far short of the requirement in the face of rising blood sugar level. These findings indicate that there is a combination of a low secretory rate and a relative insulin resistance in diabetics.
Diabetic syndrome has been described as a heterogenous one with two basic etiological lesions; one with a beta cell disorder and second resistance to the effectiveness of insulin on peripheral tissues such as muscles and the liver fast (Arky, 1978; Shervin and Felig, 1978). These views are supported by the observations in this study.
Fifty percent of maturity onset diabetics in Pakistan are overweight and the role of liver disease in the etiology of diabetes has not been established (Haider et al., 1975). Low secretary rate and insulin resistance have both been observed in diabetics in this country.

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