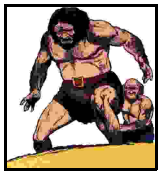

ORIGINAL PROF-564

OBESITY INDICES AND ORAL HYPOGLYCEMIC DRUGS RESPONSE

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ABSTRACT

The present study was planned to correlate obesity parameters (i.e. body mass index, waist to hip ratio and percentage body fat) with dosages of oral hypoglycemic drugs for good control in type 2 diabetes mellitus patients. Seventy patients (32 males and 38 females) attending Diabetic Clinic of Sheikh Zayed Hospital Lahore were included in the study. Thirty four patients were classified as obese and 36 as non obese on the basis of percentage body fat. No significant difference in waist/hip ratio, body mass index, fasting and post prandial glucose level was seen between obese and non obese patients. Age of 57 out of 70 diabetic patients was >40 years and half of them were seen to be obese. Obese patients above 40 years had significantly high BMI as compared to non obese patients. Forty four (63%) patients showed good control, 17 (24%) had bad control while 9 (13%) were of borderline control of diabetes. Among good control patients, non-obese subject showed significantly ($p<0.01$) lower incident of increase waist to hip ratio and higher BMI while bad control and borderline subjects showed non-significant distribution. Fasting and postprandial glucose levels of both good control-obese and bad control obese patients were significantly higher as compared to non-obese patients. All the 70 patients in the present study were on hypoglycemic drugs, 11 patients (4 obese and 7 non-obese) on sulfonylurea showed good control on low dosage, whereas good control was seen in 33 patients on high dosage metformin and combination therapy of sulfonylurea and metformin irrespective of obesity of the patients, indicates insulin resistance. Thus insulin resistance may be due to some other factors rather than the obesity and failure of release of insulin.

INTRODUCTION

Type 2 diabetes mellitus is a metabolic disease characterized by insulin resistance and hyperglycemia often associated with hypertension, lipid disturbance and obesity. The underlying pathology of type 2 diabetes mellitus appears to be increasing resistance either due to abnormal insulin structure, receptor defects, anti-insulin or anti-receptor antibodies or higher concentration of insulin antagonists[1]. Most patients of type 2 diabetes mellitus are over 40 years age and obese, polyuria and polydipsia being common symptoms. Ketonuria and weight loss generally are uncommon at the time of diagnosis[2,3].

It has been observed that obesity predisposes to type 2 diabetes mellitus, by causing insulin resistance[4,] . It has also been reported that in obese type 2 diabetic patients, besides peripheral insulin resistance there are diminished pancreatic reserves or secretory defect in the pancreatic beta cells, resulting in a failure to respond normally to elevated glucose levels[5].

Many oral drugs have been developed which either enhance release of insulin from pancreas or act peripherally, reducing the level of blood glucose. Till 1997, FDA (Food and Drug administration) approved 4 classes of oral hypoglycemic drugs[7] . These are : sulfonylureas (by stimulating pancreas to secrete more insulin) , biguanides (by combined effect of reduced

intestinal glucose absorption, decreased gluconeogenesis, increased anaerobic glycolysis and enhanced muscle uptake of glucose), alpha glucosides inhibitors (by delaying the digestion of complex carbohydrates)[8] and insulin sensitizers (thiazolidinediones) (by reducing insulin resistance in peripheral tissues[7].

Obesity may be defined as a condition, in which there is excessive amount of fat[9]. It is determined by measurement of body mass index (BMI), waist/hip ratio and percentage body fat.

BMI is the body weight (in kilograms) divided by height (in meter squared). It has been reported that there is an international consensus that 20-24.9 is a desirable range, BMI> 25 is overweight or obese[10].

Waist to hip ratio greater then 0.8 in women and greater than 0.9 in men indicate abnormal fat distribution and had greater risk of diabetes and obesity[9,11,12].

Obesity is also estimated by percentage body fat by measuring of skin fold thickness in different areas, particularly around triceps, biceps subscapular and suprailliac. Percentage body fat can be determined from the standard nomograms. In males > 20% body fat and in females > 30% body fat is considered to be obese[13].

In the presence of insulin resistance requirement for hypoglycemic drugs for proper control of blood glucose levels is expected to be higher. However, no study in Pakistan, on effect of obesity, on dose requirement of oral hypoglycemic drugs are available, nor any data about insulin resistance due to obesity has been reported from Pakistan.

Thus the present study has been planned to correlate the dosage of oral hypoglycemic drugs needed for good control of type 2 diabetes mellitus with obesity parameters i.e. body mass index, waist to hip ratio and percentage body fat.

SUBJECTS & METHODS

Seventy already diagnosed type 2 diabetic subjects (32 males and 38 females) on oral hypoglycemic drugs were included in the present study.

Blood samples of each patient (fasting and postprandial (after two hours breakfast and oral drugs) were taken in EDTA fluoride tubes and plasma preserved for glucose estimation.

Glucose was determined by enzymatic method, GOD-PAP method, (SERA-PAK Glucose KIT)[14].

Twenty three (33%) patients were on sulfonylurea, 18 (26%) on Metformin and 29 (41%) on combination of sulfonylurea and metformin. Patients on 1½ tablets of sulfonylurea or metformin or 1½ tablets sulfonylurea and one tablet of metformin were classified as low dosage.

Patients having fasting glucose level of < 140 mg/dl and postprandial glucose level of <200 mg/dl were classified as good control of diabetes. Patient showing both fasting and postprandial glucose level above good control levels was taken as bad control, while patient showing one of the value above good control level were classified as control.

RESULTS & DISCUSSION

Out of total of seventy diabetic patients 34 were classified as obese and 36 as non obese on the basis % body fat. Mean age of non obese patients was significant (P>0.01) higher as compared to obese group (table I).

Out of obesity parameters only mean % body fat was significantly (P<0.001) higher in non obese group while BMI only showed a non significant increase (table I).

Table-I. Age body mass index (BMI) waist to hip ratio (W/H) percentage body fat, fasting and postprandial glucose levels in obese and non obese male and female diabetic patients. Figures in parenthesis indicated the number of patients.

Age yrs	BMI Kg/m2	W/H Ratio	% body Fat	FGL mg/dl	PPGL mg/dl
Obese (34)					
44 ±1.59	22 ±0.6	0.89 ±0.007	2.27 ±0.97	147 ±9.39	194 ±8.94
Non-Obese (36)					
**51 ±1.77	20.16 ±0.55	0.88 ±0.008	*18.83 ±1.01	150 ±10.26	192 ±10.61
*P<0.001, **P<0.01					

Table-II. Age body mass index (BMI) waist to hip ratio (W/H) percentage body fat, fasting and postprandial glucose levels of obese and non obese male and female diabetic patients. Figures in parenthesis indicated the number of patients (up to 40 and above 40 years)

Age yrs	BMI Kg/M2	W/H Ratio	%body Fat	FGL mg/dl	PPGL mg/dl
Obese patients upto 40 years(5)					
37 ±1.53	22.1 ±1.22	0..85 ±0.013	25.88 ±2.66	126 ±17.71	167 ±16.76
Non-Obese patients up to 40 years (8)					
38 ±1.035	21.1 ±1.001	0.83 ±0.021	20.26 ±2.51	139 ±16.91	157 ±18.44
Obese patients above 40 years 29)					
5 ±1.44	21.9 ±0.59	0.85 ±0.008	28.67 ±1.037	151 ±10.52	197 ±9.92
Non-obese patients above 40 years (28)					
53 ±1.15	19.78**±0.72	0.85 ±0.008	18.42*±1.082	127 ±6.67	183 ±11.07
*P<0.001, ** P<0.05					

Higher age group of non obese subject could be due to longer standing of diabetes with weight decrease due to either dietary measures or longer period of uncontrolled diabetes. In the present study no difference in waist/hip ratio was seen between two groups (obese and non-obese) although different workers[12] have emphasized that greater waist/hip ratio may be independent risk factor of diabetes. Steven et al had also reported that % body fat being a more consistent index of obesity and diabetic risk than BMI and waist/hip ratio[15].

In the present study mean fasting and 2 hours postprandial blood glucose levels in obese and non obese patients were 147 ±9.39 mg/dl, 194 ±8.94 mg/dl and 150 ±10.26 mg/dl, 192 ±10.6 mg/dl respectively and no significant difference was noted between two groups (table I). Neither there was any significant difference in glucose levels in older (>40 years) and younger subjects (<40 years) table II. BMI & % body fat of obese subjects > 40 years age was significantly (P<0.01 and P<0.05 respectively) higher table II. In general obesity could not be related to the control states of diabetes table III. Obese good control patient showed significantly P<0.05) higher fasting and postprandial glucose levels when compared with non obese good control patients.

Table-III. Fasting and postprandial glucose level (Mean and ± S.E) of obese and non-obese diabetic patients taking oral hypoglycemic drugs and their good bad and borderline control are given. Figs in parenthesis indicated number of patients.

Control	Group	FGL mg/dl	PPGL mg/dl
Good control (44)	Obese (21)	123±4.32	167±5.10
	Non obese(23)	103*±4.81	147**±7.20
Bad control (17)	Obese (10)	198**±24.23	255****±16.20
	Non-obese (7)	162***±15.10	253***±25.46
Borderline control(9)	Obese (3)	150****±3.17	179±6.64
	Non-Obese(6)	151±5.19	180*****±11.87

* P<0.05 as compared to obese good control patients, ** P<0.01 as compared to obese good control patients,
*** P<0.001 as compared to non-obese good control patients, **** P<0.001 as compared to obese good control patients,
***** P<0.05s as compared to non-obese good control patients

Table-IV. Percentage and number of obese and non obese diabetic patients with their waist to hip ratio and body mass index with respect to their good bad and borderline control.

	Obese 34 (49%)			
	Waist to hip ratio		Body mass index	
	Low 11 (32%)	High 23(68%)	Low 11 (32%)	High 23(68%)
Good control 21	5	16	5	16
Bad control 10	5	5	5	5
Borderline control 3	1	2	1	2
	Non-obese 36 (51%)			
	Waist to hip ratio		Body mass index	
	Low 22 (61%)	High 14 (39%)	Low 32 (89%)	High 4(11%)
Good control 23	16*	7	23	-
Bade control 7	4	3	5	2
Borderline control 6	3	3	4	2
	*P<0.01			

It has been earlier reported[16] that obese diabetic have significantly higher fasting and postprandial glucose levels.

Among good control patients non obese subjects showed significantly (P<0.001) lower incident of both increased waist hip ratio and higher BMI table IV, while bad control and borderline subjects showed non significant distribution when compared according to low and high waist to hep ratio and BMI thus it appears that bad control is not related to obesity but may be due to inadequate dosage of hypoglycemic drugs and this study has already been reported[17] (Table IV)

Table-V. The number and percentage of diabetic patients with percentage body fat showing their respective dose level and control

Obese 34 (49%)		Level of dose of oral hypoglycemic drugs		Non-obese 36 (51%)		Level of dose of oral hypoglycemic drugs	
		Low (4)	High (30)			Low (10)	High (26)
Good control	21	4	17	Good control	23	7	16
Bad control	10	-	10	Bad control	7	3	4
Borderline control	3	-	3	Borderline control	6	-	6

Table-VI. The number of obese and non obese diabetic patients with low or high doses of oral hypoglycemic drugs showing good bad or borderline control is given.

Sulfonylurea 23 (33%)							
	Obese 8				Non-obese 15		
Group		Low dose 4	High dose 4	Group		Low dose 4	High dose 4
Good control	6	4	2	Good control	8	7	1
Bad control	1	-	1	Bad control	4	3	1
Borderline control	1	-	1	Borderline control	3	-	3
Metformin 18 (26%)							
	Obese 11				Non obese 7		
Group		Low dose	High dose 11	Group		Low dose	High dose 7
Good control	7	-	7	Good control	6	-	6
Bad control	4	-	4	Bad control	1	-	-
Borderline control	4	-	-	Borderline control	1	-	1
Sulfonylurea plus Metformin 29 (41%)							
	Obese 15				Non obese 14		
Group		Low dose	High dose 15	Group		Low dose	High dose 14
Good control	8	-	8	Good control	9	-	9
Bad control	5	-	5	Bad control	3	-	3
Borderline control	2	-	2	Borderline control	2	-	2

Obesity does not appear to be related to increased insulin resistance as almost equal number of obese[17] and non-obese [16] subjects required high dosage for good control (table V).

However it has been earlier reported by many workers[18,19] that type 2 obese patients respond high dosage of oral hypoglycemic drugs due to insulin resistance.

Seven out of 8 good control non-obese diabetics were on low dosage of sulfonylureas (Table VI). While all 7 obese diabetic patients and 6 non obese diabetics showed a good control on high dosage of metformin (Table VI) and 4 obese diabetic subjects showed a bad control even on high dosage metformin (Table VI).

All 29 patients on combination therapy in the present study were on high dose of sulfonylurea and metformin (Table VI) with 8 obese and 9 non obese showing a good control.

It appears that all combination therapy patients originally belong to insulin resistance, thus needing high dosages of oral hypoglycemic drugs.

Smith and Aronson[20] have reported a better control of hyperglycemia by combination therapy in patients who do not respond to even high dosage of sulfonylureas. Thus it can be concluded that bad control of the patient could not be related to obesity, rather it reflects under dosage of oral hypoglycemic drugs.

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CORRECTION

The amendment of The Professional Vol: 08, No. 1 (PROF-498) Page 146 is as under.

INCORRECT

ORIGINAL **PROF-498**

ADULT ALBINO RATS;
STUDY OF MOTOR UNITS INNERVATED BY TIBIAL NERVE

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