

## Role of Pioglitazone and Glibenclamide in Type 2 Diabetes Mellitus (NIDDM) Patients

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### ABSTRACT

**Objective:** Study was planned to examine and compare the effects of oral antidiabetic drugs in Type 2 Diabetes Mellitus patients.

**Design:** Prospective and comparative study

**Place and duration of study:** Study was conducted at the department of Pharmacology, Basic Medical Sciences Institute (BMSI) in collaboration with Medical Department Jinnah Post-graduate Medical Centre (JPMC) Karachi, from January 2006 to July 2006.

**Patients and methods:** Sixty newly untreated Type 2 Diabetes Mellitus patients were enrolled in the study. Females and Males patients were divided in two groups. In group I patients (n=27) were treated with drug pioglitazone 15 mg after meal. In group II (n=33) patients were treated with drug glibenclamide 5mg early morning just before break fast. Both drugs were given for over all study period. No titration of dose was needed. Patients with peptic ulcer, renal diseases, hepatic diseases, blood disease, any serious complications were excluded from the study. General Physical examination, pulse, blood pressure, routine investigation, etc recorded at the time of patients enrolment and same assessments taken on day 45 and day 90. Fasting Blood Sugar, and Random Blood Sugar was calculated by Glucose-Oxidase Enzymatic Method. Procedure was explained to patients and written consent was obtained on Proforma especially designed for research. Data were expressed as the Mean±SEM at the end of study and was analysis by paired t test.

**Results:** Out of 70 type 2 Diabetes Mellitus patients 60 patients were completed over all study period. Two patients withdrew from one group; i.e. drug glibenclamide group due to adverse effects like hypoglycemia. Difference between two groups at the end of study shows better results in parameters. In parameter FBS At day-0 mean value was 188.42±12.05 mg/dl At Day 45 168.45±10.99 mg/dl At Day 90 140.06±5.68 mg/dl. P Value from day-0 to day-90 was <0.05\* which was significant. In parameter RBS At Day-0 mean value was 284.18± 17.03 mg/dl At Day-45 220.12±13.39 At Day-90 170.94±5.80 mg/dl. P Value from day-0 to day-45 was <0.005\*\* which is moderately significant and from day-45 to day-90 P value was <0.002\*\* which is also moderately significant result in group II with drug glibenclamide.

**Conclusion:** Finally we concluded from this study that drug glibenclamide controlled Type 2 Diabetes Mellitus by decreasing blood sugar level in a given study period as compared with other study drug, pioglitazone.

**Key words:** FDA, TZD, S, NIDDM, IDDM

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### INTRODUCTION

Greek and Roman Physicians used the term 'diabetes' to refer to conditions in which the cardinal finding was a large urine volume<sup>1</sup>. There are two main types of diabetes mellitus type I diabetes previously known as insulin-dependent diabetes mellitus (IDDM), type II diabetes previously known as non-insulin-dependent diabetes mellitus (NIDDM)<sup>2</sup>. Type-I Diabetes mellitus is characterized by insulin deficiency and a tendency to develop ketosis where

as the type 2 diabetes mellitus is a heterogeneous group of disorders characterized by variable degrees of insulin resistance, impaired insulin secretion, and excessive hepatic glucose production<sup>3</sup>. Type 2 diabetes is more common than type I diabetes<sup>4</sup>. Type II diabetes is also referred to as non-insulin dependent diabetes (NIDDM) or adult-onset diabetes. In 1962 it was proposed that there are certain individuals who respond to the ingestion of food, by producing insulin at a 'greater-than-normal availability' it was known at that time that it was a specific type of diabetes, which would later be known as Type II Diabetes<sup>5</sup>. Type 2 Diabetes usually has no symptoms, but in the long term it can lead to excessive thirst, frequent trips to the toilet to pass

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urine and weight loss<sup>6</sup>. Incidence and prevalence of type 2 diabetes is rapidly increasing in westernized societies<sup>7</sup>. Type 2 diabetes is the most common clinical form of diabetes. Type 2 Diabetes is predicted to affect more than 320 million individuals by 2025. The greatest increase in type 2 diabetes will be in 45-64 years old individuals in developing countries<sup>8</sup>. The two metabolic defects that characterize type 2 diabetes are (a) a decreased ability of peripheral tissues to respond to insulin (insulin resistance) and (b)  $\beta$ -Cell dysfunction that is manifested as inadequate insulin secretion. In most cases, insulin resistance is the primary event and is followed by increasing degrees of  $\beta$ -cell dysfunction<sup>9</sup>. At present, when lifestyle changes fail to reduce blood glucose levels to the desirable range, the conventional approach is to begin with an oral anti hyperglycemic agent, in which we assessed the efficacy of these drugs, both as mono therapy and in combination, and discussed evidence based treatment strategies. Oral anti hyperglycemic drugs are approved by the U.S. Food and Drug Administration (FDA)<sup>10</sup>. The researchers urge clinicians to screen those with type 2 diabetes<sup>11</sup>. New Oral medications make these targets easier to achieve, especially in patients with recently diagnosed diabetes Pioglitazone, Rosiglitazone (TZD'S), help the patient's own insulin control glucose levels and allow early treatment with little risk of hypoglycemia<sup>12</sup>. Glibenclamide (Sulfonylureas) are oral drugs that stimulate the pancreas to release insulin for adequate control of blood glucose levels. The drugs should only be taken 20 to 30 minutes before a meal<sup>13</sup>.

## PATIENTS AND METHODS

After scrutinized, 70 newly untreated, Type II Diabetes Mellitus (NIDDM) patients were selected in the study. Out of 70 patients, 10 patients discontinued to take drug due to side effects and low compliance. Remaining 60 patients completed over all study period. This study was conducted at the department of Pharmacology and therapeutic Basic Medical Sciences Institute Jinnah Postgraduate Medical Centre Karachi with collaboration of Medical Department. Patients were selected from Filter Clinic (OPD) of Medical Department. Duration of study was seven months i.e., from January 2006 to July 2006. Patients were divided in to two groups. In group-I having 27 patients, in group II 33 patients were selected for further study. Patients with peptic ulcer, cardiac diseases, hepatic diseases, blood disorders any serious complicated diseases were excluded from the study. Initially history and detail clinical

examination was taken from all the participants. After explaining the limitations and related information to patients written consent was obtained from all patients. The study period was 90 days, with fortnightly follow up visits. The required information such as name, age, sex, occupation, address, previous medications, surgery, date of follow up visits etc, of each participants was recorded on the written proforma especially designed for this research. All the base line investigations was taken on the day of enrollment in the study Day 0, and similar assessments was taken on the day 45 and day 90 as per research design and protocols. After fulfilling all necessary initial requirements of patients in group I prescribed drug pioglitazone 15 mg once daily dose given after meal, group II patients were treated with glibenclamide 5mg drug once daily early morning just before break fast for over all study period. Patients were called for check up of blood pressure, pulse, weight, general physical appearance and laboratory tests. No titration of dosage of drug required during study period. FBS and RBS were calculated by Glucose-Oxidase Enzymatic Method. Specimen was collected for blood sugar in disposable 5cc syringe under aseptic environments. Data were expressed as the Mean $\pm$ SEM and 't' test was applied to determine statistical significance as the difference. Probability value of <0.05 was the limit of significance.

## RESULTS

Out of seventy,60 patients completed over all study period. Tables show base line and post treatment values. When results summed up and the test parameters were compared it was seen that after completion of study with drug pioglitazone in group I in parameter FBS at day-0 their mean value was 172.7 $\pm$ 13.32 mg/dl at day-45 165.04 $\pm$ 8.98mg/dl at day-90 153.37 $\pm$ 7.59mg/dl and in parameter RBS at day-0 mean values were 285.11 $\pm$ 15.32mg/dl at day-45 279.78 $\pm$ 13.63mg/dl at day-90 255.56 $\pm$ 12.65mg/dl. P- Value from day 0 to day 45 and from day 45 to day 90 was P>0.05 which is not significant. In group II with drug glibenclamide in parameter FBS at day-0 mean values were 188.42 $\pm$ 12.05 at day-45 168.45 $\pm$ 10.99mg/dl and at day-90 140.06 $\pm$ 5.68mg/dl. In parameter RBS at day-0 mean values were 284.18 $\pm$ 17.03mg/dl at day-45 and 220.12 $\pm$ 13.39mg/dl at day-90 170.94 $\pm$ 5.80mg/dl. P value from day 45 to day 90 was significant (P<0.05). In parameters RBS from day 0 to day 45 P Value was <0.005 and from day 45 to day 90 P value was <0.002\*\* which is moderately Significant on drug glibenclamide which shows significant changes and decreased blood sugar level in a given study period.

## ORIGINAL ARTICLE

Table 1: Different patients with percentage and P Value on Pioglitazone and Glibenclamide groups.

	Group:I Drug	=n	% age	Group II Drug	=n	% age	P Value
Females	Pioglitazone	16	59.3	Glibenclamide	20	60.6	0.916
Males	Pioglitazone	11	40.7	Glibenclamide	13	39.41	

Key: (= n) indicates Number Of Patients. (% age) indicates Percentage among Two Groups. P Value: 0.916

Table 2: Changes in parameter fasting and random blood sugar of patients on Pioglitazone group(n=27).

Parameter	At Day 0	At Day 45	At Day 90	P Value	
FBS mg/dl	172.7±13.32	165.04±8.98	153.37±7.59	Day0today45	Day45today90
				>0.05	>0.05
RBS mg/dl	285.11±15.32	279.78±13.63	255.56±12.65	>0.05	>0.05

Key: (±) Indicates standard error of mean. P value >0.05 is Non Significant.

Table 3: Changes in parameter fasting and random blood sugar of patients on Glibenclamide group(n=33).

Parameter	At Day 0	Day 45	Day 90	P Value	
				Day0today45	Day45today90
FBS mg/dl	188.42±12.05	168.45±10.99	140.06±5.68	>0.05	<0.05*
RBS mg/dl	284.18±17.03	220.12±13.39	170.94±5.80	<0.005**	<0.002**

Key: All Values Are Expressed in MEAN±SEM.(±) Indicates SD Of Mean. P Value <0.05\* Significant. P Value <0.005 Moderate Significant.

## DISCUSSION

Objective of our study was planned to examine and compare the effects of oral anti diabetic drugs in type 2 diabetes mellitus patients among both groups. Glibenclamide drug appears good in decreasing blood glucose level during given study period after comparing of both drugs results. With drug glibenclamide in parameter FBS at day-0 was 188.42±12.05mg/dl at day 45 168.45±10.99mg/dl and at day-90 it reduced to 140.06±5.68mg/dl, P value from day 0 to day 45 was >0.05, at day-45 to day-90 P Value was < 0.05 which was significant at the end of study. In parameter RBS at day 0 mean value was 284.18±17.03mg/dl, at day 45 220.12±13.39mg/dl and at day 90 it was 170.94±5.80. P value from day 0 to day 45 was <0.005 (moderately significant) and from day 45 to day 90 P value was <0.002\*\* (moderately significant). These results correlate with the results of Alvarsson M et al<sup>14</sup> study that fasting blood glucose level versus base line was lower than in both groups especially with our study drug glibenclamide (P<0.05, significant). Jr Clark CM al<sup>15</sup> study results also match with our study glibenclamide. The drug decreases blood glucose level in a given study period with P <0.05 (Significant). Another study by Aronoff S et al<sup>16</sup> is contrast with our study results. Difference from our study was that they selected different race (species) patients e.g., most (78%) patients were Caucasian, 12% were Hispanic,8% were African-American, 2% were Asian. In our study only Asian species (100%) were included. Drug pioglitazone group I in parameter FBS from day 0 to 45 day 45 to day 90 P value was > 0.05. In parameter RBS day 0 it was 285.11±15.32mg/dl, at day 45 it reduced to

279.78±13.63 mg/dl and at day 90 it was 255.56±12.65 mg/dl. Day-0 to day-45 P value was >0.05. Day 45 to 90 P value was >0.05 (non significant). Our study results match with the study results of Diani AR et al<sup>17</sup> that proved that pioglitazone slow the progression of type 2 diabetes by preserving pancreatic β –cells. In our study drug pioglitazone showed slow progression on type 2 diabetes. Gillies interventions in all the meta analysis give improvements to pharmacotherapy with good controlling of other risk factors for example: obesity, smoking, physical inactivity life style less work more in take of fatty diet etc. In our study glibenclamide group patients, strictly follow our guidelines and instructions related with the risk factors so the results were good in a given study period as compared with the other drug pioglitazone (group I). Gress TW et al<sup>18</sup> study was in contrast with our study. Difference in these two studies was due to research methodology. Langer O et al<sup>19</sup>, given a remarkable conclusion related with safety and efficacy of drug glibenclamide that proved clinically effective alternative to insulin in gestational diabetes women. Reynolds TM<sup>20</sup> study describes that good evidence exists about complications in diabetes that are improved by its better control. Drop out patients from our study were only 10 which proved good compliance of the drug.

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