ORIGINAL ARTICLE

Role of Oral Antidiabetic Agents in Type-2 Diabetes Mellitus Patients

RAJ KUMAR CHOHAN, JAGDESH KIMAR, SHAH MURAD

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 Postgraduate Medical Centre (JPMC) Karachi, from January 2006 to July 2006.
Patients and methods: After scrutinized sixty newly untreated type 2 Diabetes Mellitus patients were enrolled in this study. Females and Males patients were divided in two groups. In Group-I(n=27)patients were treated with drug pioglitazone 15mg after meal. In group-II (n=33) patients were treated with drug glibenclamide 5mg early morning just before breakfast. Patients with peptic ulcer, renal diseases, hepatic diseases, blood diseases, any serious complications were excluded from this study. General Physical examination, pulse, blood pressure, routine investigation etc. was recorded at the time of patients enrollment and same assessments was taken at day 45 and at day 90. Fasting and Random Blood Sugar was calculated by Glucose-Oxidase Enzymatic method. Procedure was explained to patients and written consent was obtained on proforma which was especially designed for research. The data were expressed as the Mean$\pm$SEM at the end of study and was analysis by paired "t" test.
Results: Difference between two groups at the end of study shows better results in given parameters. FBS Parameter at day 0 mean values were 188.42$\pm$12.05mg/dl at day 90 140.06$\pm$ 5.68mg/dl. P value from day 0 to day 90 was P<0.05*(Significant). In parameter RBS at day 0 mean values were 284.18$\pm$17.05mg/dl and at day 90 170.94 $\pm$ 5.80 mg/dl. P-Value from day 0 to day 45 was P<0.005**(Moderate significant) and from day 45 to day 90 P-value was P<0.002**(Moderate Significant),better results obtained from group-II with drug glibenclamide at the end of study.
Conclusion: Drug glibenclamide controlled type-2 diabetes mellitus by decreasing blood sugar level in a given study period as compared with other our study drug pioglitazone.
Key words: Type 2 diabetes mellitus. University Group Diabetes Programme. Oral antihyperglycemic medication. Fasting plasma glucose.

INTRODUCTION

The term "diabetes" was first coined by Araetus of Cappodocia (81-133AD). Later, the word Mellitus (honey sweet) was added by Thomas Willis (Britain) in 1675 after rediscovering the sweetness of urine and blood of patients[1]. With diabetes mellitus, carbohydrate, fat and protein metabolism are impaired because of a deficient response to insulin[2]. Type-1 diabetes is related to loss of insulin secreting cells in the pancreas. Type-2 diabetes is related to target cell resistance to the action of insulin[3]. Type-2 diabetes is characterized by insulin resistance and progressive beta cell failure[4]. The incidence of childhood diabetes has increased in Europe and many other parts of the world over the past 20-30 years[5]. In Sub-saharan Africa, the prevalence and burden of type-2 diabetes are rising quickly[6]. Type-2 diabetes mellitus is one of the most common chronic disease in the U.K.[7]. Patients with type-2 diabetes often have many associated disorders, including hypertension, obesity, hyperlipidemia and accelerated atherosclerosis[8]. Dietary guideline for diabetes, which emphasize moderation of fat and sugar intake, increased fruit and vegetables and salt restriction[9]. The standard approach at initial diagnosis for many patients with type-2 diabetes is a prescription of diet and physical activity to correct their hyperglycemia. When glycemic targets cannot be attained or maintained with this approach, an oral anti-hyperglycemic medication is added to the lifestyle regimen[10]. The underlying insulin resistance

---

Department of Pharmacology, Bhittai Dental & Medical College Mirpurkhas.
Department of Pharmacology, Lahore Medical & Dental College, Lahore
Correspondence to Dr. Rajkumar Chohan, Assistant Professor Email: rajkumarchohan655@gmail.com

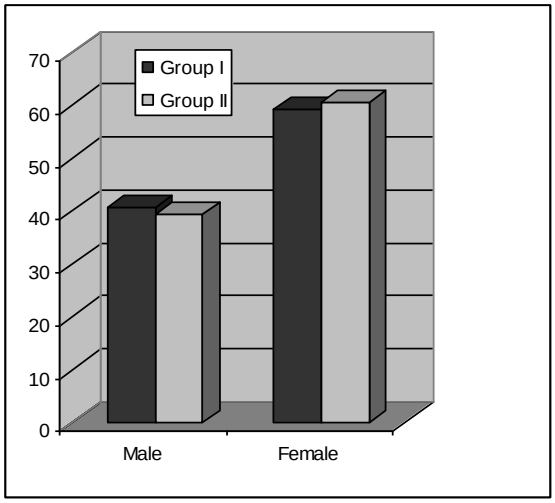
and impaired insulin secretion in patients with type-2 diabetes worsen over time, necessitating the use of increasingly powerful drugs often in combination, to control glycemic levels[11]. Sulphonylureas put more insulin into blood stream, the insulin helps to lower blood glucose[12]. Thiazolidinediones commonly called glitazones. They lower blood glucose by increasing the sensitivity of body's cells to insulin[13]. Pioglitazone is approved as a monotherapy and in combination with metformin, Sulfonylureas, and insulin for the treatment of type-2 diabetes[14].

PATIENTS & METHOD

After scrutinized only 60 patients newly untreated, Type II Diabetes Mellitus (NIDDM) Patients were selected in this study out of 70 patients, 10 patients discontinued to take drug due to side effects and low compliance. Remaining 60 patients were 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 Medical Department. Patients were selected from Filter Clinic (OPD) of Medical Department from January 2006 to July 2006. Patients were divided in to two groups in group I having (n=27) patients, in group II (n=33) patients newly untreated Type 2 Diabetes Mellitus of either Sexes males and females having different ages ranges from 02 to 70 years. Patients with peptic ulcer, cardiac diseases, hepatic diseases, blood disorders any serious complicated diseases were excluded from this 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 main study period was consisted on 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 at 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, patients was reassured after listening their point of view. Drug compliance to the regimen was monitored by interview and counseling at each clinical visit. No titration of dosage of drug was required during study period. FBS and RBS was 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 ± SEM and `t` test was applied to determine statistical significance as the difference. Probability value of "<0.05" was the limit of significance.

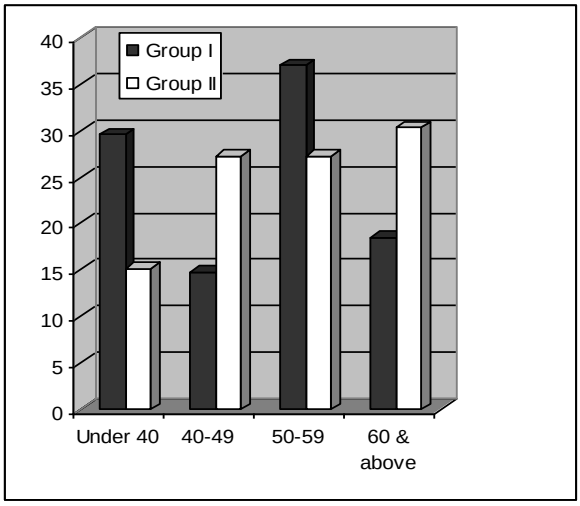
RESULTS

Graph 1: Characteristics of the patient gender wise, with percentage on pioglitazone group-I and glibenclimade group-II patients.



Key: %age: indicates percentage among groups. n: indicates number of patients in groups.

Graph 2: Characteristics of the patient age wise, with percentage on pioglitazone group-I and glibenclimade group-II patients.



Key: % age: indicates percentage among groups. n: indicates number of patients in groups.

Out of seventy type-2 diabetes mellitus patients, 60 patients completed over all study period. Tables show the baseline and post-treatment values. When results were summed up and the test parameter was compared, it was seen that drug glibenclamide decreasing blood sugar level in type-2 diabetes mellitus in a given time period. In Group-I, total number of patients were (n=27) females patients were 16 (59.3%) and males patients were 11 (40.7%). And in glibenclamide group-II, total number of patients were (n=33) females patients were 20 (60.6%) and males patients were 13 (39.4%). Difference between two groups at the end of study showed better results in given parameters with glibenclamide group II patients. In FBS Parameter at day 0 mean value were 188.42 ± 12.05mg/dl at day 90 140.06 ± 5.68mg/dl. P value from day 45 to day 90 was P<0.05*(Significant). In parameter RBS at day 0 mean values were 284.18 ± 17.05mg/dl and at day 90 170.94 ± 5.80 mg/dl. P-Value from day 0 day 45 was P<0.005**(Moderate significant) from day 45 to day 90 P-value was P<0.002**(Moderate Significant) results of group-II with drug glibenclamide. At the end of study we obtained better result from glibenclamide group-II patients.

Table 1: Different patients with percentage and P value on pioglitazone group I Patients. Pioglitazone Group-I (n=27)

Gender	Drug given	=n	%age
Female	Pioglitazone	16	59.3
Male	Pioglitazone	11	40.7

Key: =n indicates number of patients. %age indicates percentage among two groups. Pvalue : 0.916

Table 2: Different patients with percentage and P value on Glibenclamide group-II Patients. Glibenclamide Group-II (n=33)

Gender	Drug given	=n	%age
Female	Glibenclamide	20	60.6
Male	Glibenclamide	13	39.4

Key: =n indicates number of patients. %age indicates percentage among two groups. P value : 0.916

T able 3: Changes in parameter fasting and random blood sugar on Glibenclamide Group-II patients.Glibenclamide Group-II (n=33)

Parameter	At day 0	At day 90	P-Value	
			Day 0 to Day 45	Day 45 to Day 90
FBS mg/dl	188.42 ±12.05	140.06±5.68	>0.05	<0.05*
RBS mg/dl	284.18±17.05	170.94±5.80	<0.005**	<0.002**

Key: ± indicates standard error of mean. P value : <0.05* (Significant). P value : <0.005** (Moderate Significant). P value : <0.002** (Moderate Significant).

DISCUSSION

Rachman J, Levy JC, Barrow BA et al[15] study was in accordance with our study, according to their study, sulfonylureas therapy substantially reduced fasting plasma glucose concentrations, compared with diet therapy alone. Some differences was obviously present in both studies. Engler RL & Yellon DM[16] study in which (UGDP) assessed the efficacy of oral hypoglycemic treatment in comparison with insulin and diet alone in the prevention of vascular complications. This concluded study work initiate a positive support to one of our given study oral hypoglycemic drug glibenclamide. Our study results on glibenclamide group-II patients, in given parameters. FBS Parameter at day 0 mean values were 188.42±12.05mg/dl at day 90 140.06 ± 5.68mg/dl. P value from day 45 to day 90 was P<0.05*(Significant). In parameter RBS at day 0 mean values were 284.18±17.05mg/dl and at day 90 170.94±5.80 mg/dl. P-Value from day 0 to day 45 was P<0.005**(Moderate significant) and from day 45 to day 90 P-value was P<0.002**(Moderate Significant) better results were obtained from glibenclamide group-II patients. Drug glibenclamide proved good control blood sugar level in a given specific study period. Poor control on blood sugar level with pioglitazone group-I patients with certain other factors and reasons some of the important weaknesses and negligence's of their patients was observed in which sedentary life style, less physical activities, careless attitude related with their disease, poor socio-economical condition, lack of knowledge may be worsen their glycemic control. Hanefeld M et al [17]. Study goal was to assess the one year efficacy and safety of the addition of pioglitazone, metformin, to existing sulfonylureas therapy in patients with inadequately controlled type II diabetes, our study goal was shows some resemblance with this study. Another wonderful study work was done by Jarvinen H Yki[18] that with type-II diabetes is currently the only approved indication for therapy with thiazolidinediones. Our point of view was not

correlate with this approved indication because thiazolidinediones drugs not given frequently in the presence of significant liver disease are with a concurrent diagnosis of heart failure. O'Moore TM, Sullivan, Prins JB[19] clinical studies showed that ~10-25% of the patients treated with thiazolidinedione did not achieve a 15% reduction in fasting plasma glucose, this given clinical study observation was not totally in controversial with one of our given current study drug pioglitazone.

CONCLUSION

Drug glibenclamide controlled type-2 diabetes mellitus by decreasing blood sugar level in a given study period as compared with other our study drug pioglitazone.

REFERENCES

1. AM Ahmed. History of diabetes mellitus. Saudi Med J 2002; 23(4): 373-8.
2. Hall JE.Insulin, Glucagon, and Diabetes Mellitus. Pocket companion to Guyton's Medical Physiolog 2006: 604.
3. Stringer JL. Insulin, Glucagon, and oral Hypoglycemic Drugs. Basic concepts in Pharmacology 2001: 234.
4. Kaiser N, Nesher R, Donath MY. Psammomys obesus, a model for environment gene interactions in type 2 diabetes. Invited perspective article Diabetes 2005; 54 (2): 137-144.
5. Gardner SG, Bingley PJ, Sawtell PA. Rising incidence of insulin dependent diabetes in children aged under 5 years in the Oxford region: time trend analysis. BMJ 1998; 8(8): 397-398.
6. Mbanya JCN, Motala AA, Sobngwi-E. Diabetes in Sub-Saharan Africa. The lancet 2010; 375(9733): 2254-2266.
7. Davies M, srinivasan B, Glycaemic Management of type 2 diabetes. Medicine 2006; 34(2): 69-70.
8. IPP-E. New drugs for type 2 diabetes. Diabetes 2002: 1-9.
9. Hunter SJ, Bell PM. Diabetes and hypertension. Medicine 2006; 34(2): 76-79.
10. Tan MH, Baksi A, Krahulec B. comparison of pioglitazone and gliclazide in sustaining glycemic control over 2 years in patients with type 2 diabetes. Diabetes Care 2005; 28: 544-550.
11. Nathan DM. Thiazolidinediones for initial treatment of type 2 diabetes? N Engl J Med 2006; 355(23): 2477-2480.
12. BMJ Publishing group Diabetes, type 2. BMJ best treatment. BMJ clinical evidence 2007: 1-4.
13. Pip and Emis. Treatments for type 2 diabetes. Prodigy Knowledge 2006:1-6.
14. Nolte MS.Pancreatic Hormones and Antidiabetic Drugs. Oral antidiabetic agents. Basic and Clinical Pharmacology 2009: 727-747.
15. 15. Rachman J, levy JC, Barrow BA. Relative hyper proinsulinemia of NIDDM persists despite the reduction of hyperglycemia with insulin or sulfonylurea therapy. Diabetes 1997; 46: 1557-1562.
16. Engler RL, Yellon DM. Sulfonylurea KATP Blockade in type II diabetes and preconditioning in cardiovascular disease. Circulation 1996; 94: 2297-2301.
17. 17. Hanefeld M, Brunetti P, Schernthaner GH. One year glycemic control with a Sulfonylurea Plus Pioglitazone versus a sulfonylurea Plus metformin in Patients with type 2 diabetes. Diabetes Care (American Diabetes Association) 2004; 27: 141-147.
18. Jarvinen H Yki. Drug therapy. Thiazolidinediones. N Engl J Med 2004; 351:1106-18.
19. O' Moore TM, Sullivan, Prins JB. Thiazolidinediones and type 2 diabetes: new drugs for an old disease. MJA 2002; 176(8): 381-386.