International Journal of Pharmacology

ISSN 1811-7775

science alert

ansinet
Asian Network for Scientific Information

International Journal of Pharmacology 2 (3): 316-319, 2006
ISSN 1811-7775

T he First Research Challenge for Diamicron MR in Iranian Diabetic Patients

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Abstract: The aim of the present study was to test Diamicron's effectiveness in a group of Iranian patients. In a clinical trial study, 40 diabetic patients which their hyperglycemia was not controlled with diet and exercise were enrolled to take Diamicron MR for a 12 weeks period and their Fasting Plasma Glucose (FPG) and HbA1c measured during treatment. Data were analyzed by SPSS11 statistical package. Repeated measures ANOVA and Paired t tests were used to analyze data . Twenty four persons (60%) were males and 16 of them (40%) were females. The mean for age was 48.8±13.2 (SD) years. FPG in patients before starting drug treatment had a mean of 236.65±75 mg dL^{-1}. Mean of FPG for second week after start of treatment was 180±65 mg dL^{-1}. It was 152±61 mg dL^{-1} on 4th week and 136±35 mg dL^{-1} on 8th week. Mean of FPG on 12th weeks was 131±40 mg dL^{-1}. HbA1c was checked both at the beginning of treatment and at the 12th week. Its mean was 11.1±1.9 at the beginning and it was 8.6±1.6 after 12 weeks. The decrease in FPG and HbA1c during the treatment period compared to pretreatment FPG was statistically significant ($p<0.01$). Diamicron MR was effective in controlling hyperglycemia with a good compliance and less complications in Iranian patients.

Key words: Diabetes, Diamicron MR, sulfonylurea, oral anti hyperglycemic agents, Glycosylated hemoglobin

INTRODUCTION

As some other non communicable diseases diabetes especially type II diabetes which is a more common chronic diseases with a high disease burden, is considered as a major health problem.

It is going to be the 4th cause of mortality in developed countries. In Iran it has a prevalence of 7.2-12% in people over 30 years of age (Azizi, 2002). An appropriate control of disease has an important role on decreasing its complications. Several studies had shown that oral antidiabetic agents can decrease an average of 1-2% in HbA1c level (Defronzora, 2000; Buse, 1999; In Zucchi, 2002). The UKPDS and DCCT studies have shown that strict control hyperglycemia can result in a 60 percent decrease in micro vascular complications of diabetes (The Diabetes Control and Complications Trial Research Group, 1993). The UKPDS study has revealed that a 1% decrease in glycated Hb can give rise to a 35% decrease in micro vascular complications of diabetes (Prospective Diabetes Study Group, 1998).

Current oral anti-diabetic agents, although quite effective in control of disease, but have a compliance problem in long usage.

Diamicron MR is a second generation sulfonylurea which has been used in recent times for treatment of type 2 diabetes.

Diamicron MR is a sulfonylurea with unique clinical benefits. Diamicron MR is the first oral anti-diabetic agent to employ a hydrophilic matrix, which allows predictable and reproducible release of active ingredient over 24 h and hence once daily administration of it has higher compliance. Many previous studies have shown its effectiveness. But a trial research has not been conducted in Iran to test it's effectiveness in Iranian patients. The aim of study was to test its effectiveness in reducing HbA1 and glycemic level among type 2 diabetic patients.

MATERIALS AND METHODS

In a clinical trial study, the effect of Diamicron MR on hyperglycemic status in type II diabetes was investigated with 40 newly diagnosed diabetic patients whose disease couldn't be controlled by diet and exercise. A medical history was taken and anthropometric measurements were performed based on standard procedures. Physical examination was performed by a physician and data was collected via questionnaire. Patients took off their shoes for measuring both height and weight. Body Mass Index (BMI) was calculated dividing weight (kg) by height (square metes). Blood pressure was measured after 15 min of resting, by a standard mercury sphygmomanometer. Hypertension was defined as a BP >= 140/90 or a history of using drugs for hypertension.

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Plasma glucose was measured by Glucose oxidase chromatography procedure. Glycosilated hemoglobine (HbA1c) was measured using a calorimetric kit in a reliable laboratory. After measuring Fasting Plasma Glucose (FPG) and HbA1c, each patient took a 30 mg single dose of diamicron MR tablets with breakfast. Patients were visited again at second, 4th, 8th and 12th weeks. In each visit time patients were consulted for hypoglycemic symptoms and their compliance to drug and their FPG was repeated. The primary dose of drug was maintained if Fasting Plasma Glucose (FPG) was 140 mg dL^{-1} or lower. Otherwise drug dosage was increased up to a maximum of 4 tablets taken as a single dose with breakfast meal. HbA1c measurement was repeated at the end of 12th week of drug consumption. Collected data were analyzed by SPSS statistical software. Frequency table, paired t test and repeated measures ANOVA were used to analyze data.

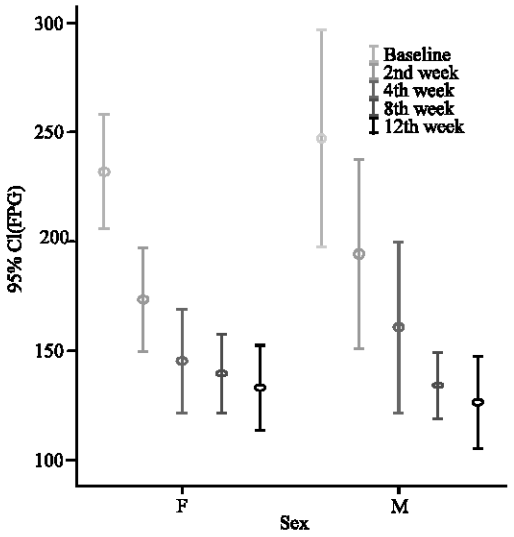

Fig. 1: Error bar diagram for FPG during treatment in males and females

RESULTS

Of all the 40 patients entered to study, 24 persons (60%) were males and 16 of them (40%) were females. They had an age range of 25-75 years and the mean and standard deviation for age was 48.8±13.2 years.

The mean for age was 53.4±11.3 years for males and 45.2±13.6 years for females .The range of BMI for patients was 21-37 with a mean of 28.2±4.5. 13 people (32.5%) were obese and 8(20%) of them were hypertensive. A positive family history for DM was found in 9 patients (Table 1).

The FPG in patients before starting drug treatment had a range of 131-444 and a mean of 236.65±75. Mean of FPG for second week after beginning of treatment was 180±65 mg dL^{-1}. It was 152±61 mg dL^{-1} on 4th week and 136±35 on 8th week. Mean of FPG on 12th weeks was 131±40 mg dL^{-1}.

Means of FPG level before and during treatment both in males and females is shown in Table 2.

No significant statistical difference was found between means of FPG in males and females and the comparison is given in Fig. 1. Histograms of FPG at the

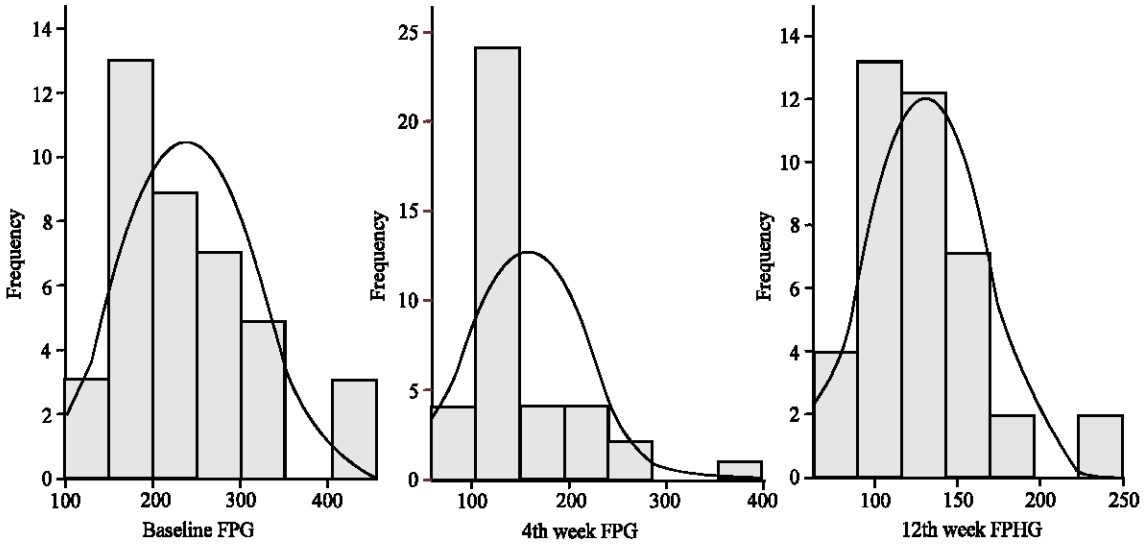

Fig. 2: Histogram of beseline, 4th week and 12th week fasting plasma glucose (FPG)

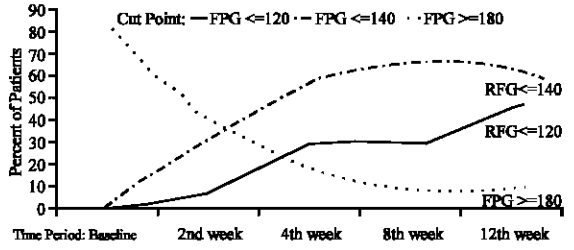

Fig. 3: Compared percents of patients with fasting plasma glucose (FPG) below or above some cut point during treatment period

Table 1: Base line characteristic features in patients enrolled to study

Characteristics	Statistics
Number of patients	40
Sex	24 males and 16 females
Age (Mean±SD)	48.8±13.2
Hypertension (%)	20
Positive family history for DM (%)	22.5
Obesity (%)	32.5
Mean baseline FPG (±SD)	236±75
Mean baseline HbA1c (±SD)	11.6±1.6

Table 2: Means of fasting plasma glucose (FPG) during the treatment period

		FPG				
Sex		Baseline	Week 2	Week 4	Week 8	Week 12
Female	N	24.0	24.0	23.0	24.0	24.0
	Mean	229.4	171.8	145.8	138.2	133.7
	SD	60.5	53.4	53.6	40.5	42.8
Male	N	16.0	16.0	16.0	16.0	16.0
	Mean	247.5	194.0	160.8	134.4	127.1
	SD	92.2	79.3	72.4	27.1	36.9
Total	N	40.0	40.0	39.0	40.0	40.0
	Mean	236.6	180.7	152.0	136.7	131.1
	SD	74.2	65.0	61.5	35.4	40.2

beginning of treatment and at the 4th and 12th week of treatment are compared in Fig. 2.

The reduction in FPG during the treatment period compared to baseline FPG was tested by Repeated measures ANOVA and Paired t test which showed all the differences to be significant ($p<0.01$).

The decrement in FPG after fourth week of treatment towards the 8th week and either the decrease from 8th to 12th week was not significant statistically. Compared percents of patients with FPG below or above given cutoff points during treatment period is shown in Fig. 3. In all patients HbA1c was checked both at the start of treatment and at the 12th week. Its mean was 11.68±1.6 at the beginning and 8.9±1.7 after 12 weeks. The difference was found statistically significant ($p<0.01$, $t = 8.01$).

Patients in this study had a very good compliance. All of the patients took their drug as prescribed and didn't have any complaints. No hypoglycemic problems were encountered.

DISCUSSION

An appropriate control of disease has an important role on decreasing its complications. Poor compliance caused by drug complications (mainly gastrointestinal) has always been a major problem with oral anti diabetic agents like biguanides or sulfonylureas. All patients in our study had an excellent compliance and no one omitted using the drug or complained of its complications. Guillausseau and Greb (2001) had similar findings with Diamicron MR in their study on diabetic patients. They found the compliance to be good without any event of hypoglycaemia Drouin (2000) also reported a good compliance for Diamicron MR. Despite the role of anti diabetic drug complications on compliance, it has been concluded that dose frequency has a major role on compliance for many drugs as well as oral anti diabetic agents (Pullar *et al*., 1988; Paes *et al*., 1997). From the results it was found that three phases of drug effect: the first phase as the first month of treatment in which there is a steep decline in percentage of those who had a FPG more than 180 g dL^{-1} and a sharp rise in percentage of those with FPG = 140 g dL^{-1}. The second phase which was a three weeks long period the changes were modest ending in a plateau state as third phase. Present findings showed that Diamicron MR is quite effective in decreasing plasma glucose from a pre treatment mean FPG of 236.6 to 131.1 g dL^{-1} at the end of 12th week. As it is obvious in Fig. 2, a homogen uncontrolled plasma glucose distribution before treatment changed to a homogen good controlled distribution of plasma glucose at the end of 12th week. The results for HbA1c decrease was also significant in our study. Previous studies outside Iran which have checked efficacy of Diamicron MR in reducing plasma glucose or HbA1c, had shown that it is as effective as other oral anti diabetic agents such as Glibenclamide and Metformin but with a better compliance and easier administration (Jennings *et al*., 1992; Tessier *et al*., 1994; Harrower, 1985; Noury and Nandeuil, 1991; Collier *et al*., 1989).

CONCLUSIONS

As previous studies outside Iran had shown, similar results were found with Iranian patients declaring that Diamicron MR was effective in controlling plasma glucose of patients with type 2 diabetes. It improved enough the HbA1c to an acceptable level. It had a good compliance outcome with no hypoglycemic problems.

ACKNOWLEDGMENT

This research was conducted by a grant from Servier (France) company and its Iranian Representative Daroudad. We are thankful to their help.

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