

Comparison Between Effect of Glimepiride and Pioglitazone on the C-Reactive Protein Level of Type 2 Diabetic Patient

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Abstract:

Background: This study was carried out to see the effect of glimepiride and pioglitazone on the serum hs-CRP level in type 2 diabetic patients.

Material and Methods: A non-blind comparative study was conducted among 70 patients with type 2 diabetes (as per WHO criteria) divided into two groups (35 each) to see the effect of glimepiride and pioglitazone on their blood hs-CRP level.

Results: 35 type-2 diabetic patients were given glimepiride. Another 35 patients were given pioglitazone. Fasting blood sugar, HbA1c %, hs-CRP and lipid profile were estimated before and 12 weeks after intervention. The mean change of serum hs-CRP was 1.13 mg/L to 0.76 mg/L in pioglitazone group. In glimepiride group the mean change of serum hs-CRP was 0.96 mg/L to 0.94 mg/L after 12 weeks. The change was greater in pioglitazone group in comparison to glimepiride group.

Conclusion: Reduction of hs-CRP was significant in the study subjects revealing its future potential in reducing the vascular complications of type – 2 diabetes mellitus.

Keyword: Type-2 diabetes, hs- CRP, Glimepiride, Pioglitazone, Cardiovascular complication

Introduction

Diabetes mellitus is a growing health problem that causes significant morbidity and mortality.¹ It is estimated that more than 3 million people are now suffering from type-2 diabetes in Bangladesh.² Certain proteins known collectively as the “acute phase response” are produced in inflammation mainly by liver. The best known of these are C-reactive protein, a beta-globulin. It is established that, in diabetes hs CRP levels are elevated.³ A recent study also proved the same in type-2 diabetic patients in Bangladeshi population.⁴ CRP is directly associated in atherosclerotic plaque formation and increases cardiovascular risks.⁵

Thiazolidinediones improve insulin sensitivity and provide durable glycemic control. They also reduce inflammatory markers, improve vascular function and lipid profiles in patients with type-2 diabetes, which may improve the long term cardiovascular outcomes.⁶ Now a good number of prospective studies are going on in the western world on these relevant field. This is the first study of this kind that has been carried out in Bangladesh. This study was done to see the baseline CRP level in type 2 diabetes patients and effect of thiazolidinediones (pioglitazone) on it.

Materials and Methods

It was a non-blind comparative study extending from January 2007 to December 2007 done in the Rajshahi Medical College Hospital and in the Rajshahi Diabetic Association Hospital. By purposive sampling method, 70 type-2 diabetic patients were included in this study. Among these 70 patients, 35 were treated with pioglitazone for 12 weeks of time and rest 35 type-2 diabetic patients were treated with glimepiride for the same time. Inclusion criteria were: age >40 yrs, patients with type 2 diabetes (as per WHO criteria) of <2 years duration. Exclusion criteria were: patients with >2 yrs duration with type 2, on insulin therapy, patients with <40 yrs of age and >60 years, smoker, alcoholic, hypertensive, congestive cardiac failure, oedema due to any cause, kidney and liver disease, pregnancy and obesity (BMI >30 kg/m²). Data was collected after taking informed consent of the patient. Blood samples were taken for fasting blood glucose (8 hour fasting), 2 hours after breakfast blood sugar, HbA1c (glycosylated haemoglobin), fasting lipid profile, hs-CRP (high sensitive C-reactive protein) at base line and after 3 month intervention. The data was analyzed with the help of SPSS software program. A p-value of <0.05 was considered as significant.

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Results

The results of the study are given in Table I-IV

Table-I
Glycemic status of the study population before and after drug intervention:

Biochemical variables	Respondent's group							
	Pioglitazone				Glimpeiride			
	Male	Female	Total	P-value	Male	Female	Total	P-value
FBS before drug (mmol/L)	10.15	9.14	9.86±3.11	<.05	6.86	8.04	7.72±1.95	.052
FBS after drug(mmol/L)	8.50	7.67	8.26±2.71		7.16	8.46	7.37±3.02	
2ABFG before drug(mmol/L)	15.93	13.18	15.14±4.99	<.05	9.57	11.07	10.21±4.34	.062
2ABFG after drug(mmol/L)	11.69	11.23	11.56±4.88		9.32	10.24	9.71±5.14	
HbA _{1c} % before drug	9.02	8.21	8.79±1.45	<.05	7.23	7.38	7.29±0.83	.067
HbA _{1c} % after drug	8.11	7.52	7.94±1.46		6.82	7.31	7.03±1.12	

Table II
hsC-RP protein distribution in the study population (before and after drug intervention):

	Respondent's group					
	Pioglitazone			Glimpeiride		
	hs-CRP before drug	hs-CRP after drug	P-value	hs-CRP before drug	hs-CRP after drug	P-value
Male	1.27	0.76		1.12	0.95	
Female	0.78	0.76		0.74	0.93	
Total	1.13±1.58	0.76±1.25	<0.05	0.96±1.59	0.94±1.50	>0.05

Table-III
Lipidemic status of the study population (before and after drug intervention):

	Respondent's group							
	Pioglitazone				Glimpeiride			
	Male	Female	Total	P-value	Male	Female	Total	P-value
HDL before drug	39	41	40±4	>.05	39	39	39±4	>.05
HDL after drug	40	40	40±4		40	38	39±4	
LDL before drug	108	131	115±32	>.05	103	120	110±25	>.05
LDL after drug	110	117	112±26		110	126	117±25	
TC before drug	200	240	211±38	>.05	184	220	200±40	>.05
TC after drug	199	230	208±40		190	222	204±34	
TG before drug	211	208	210±50	>.05	214	226	219±70	>.05
TG after drug	210	217	212±39		205	231	216±60	

Table-IV
Changes in mean body weight of the study population (before and after drug intervention):

Respondent's group	Respondent's gender	Weight before drug	Weight after drug	P-value
Pioglitazone group n=35	Male	60.68±9.886	61.68±9.835	>0.05
	Female	55.60±6.995	56.50±7.352	
	Total	59.23±9.347	60.20±9.393	
Glimpeiride group n=35	Male	59.25±11.580	59.25±11.111	>0.05
	Female	51.73±6.798	51.73±6.734	
	Total	56.03±10.402	56.03±10.095	

Discussion

In our study, we observed the effects of glimepiride and pioglitazone on the hs-CRP level, glycemic and lipidemic status of the type 2 diabetic patient. For this purpose, we enrolled 70 type 2 diabetic patients. Among them 35 were treated with pioglitazone 30mg in the morning for 12 weeks of time and rest 35 type-2 diabetic patients were treated with glimepiride (1 to 6 mg, according to the glycemic status) for the same time.

In this study the control of glycemic status was suboptimal in both group with the drug intervention, i.e. mean HbA1c% was reduced 8.79% to 7.94% in pioglitazone group and 7.29% to 7.03% in glimepiride group. Reduction of mean fasting blood sugar in pioglitazone group was 9.86mmol/L to 8.26mmol/L, whereas in glimepiride group it was reduced 7.72mmol/L to 7.37mmol/L. Though the reduction of both HbA1c% and fasting blood sugar was suboptimal, but the reduction in pioglitazone group was significant ($p < .05$) and in glimepiride group was near to significant ($P = 0.067$ and $P = 0.052$ respectively) (Table-I). The mean change of HbA1c% was 0.85% in pioglitazone group and 0.26% in glimepiride group. The change in pioglitazone group was significant ($P < 0.05$).

In this study there was change of serum mean hs-CRP level from 1.13 mg/L to 0.76 mg/L in pioglitazone group after 12 weeks of pioglitazone (30 gm) intervention and in glimepiride group who did not receive pioglitazone, the change of serum mean hs-CRP level was 0.96 mg/L to 0.94 mg/L after 12 weeks (Table-II). This change in hs-CRP in pioglitazone group in comparison to glimepiride group is statistically significant ($p > 0.05$).

Haffner SM et al. in 2002 showed that the decline in CRP was 0.155 mg/dl in placebo group, 0.52 mg/dl in rosiglitazone 8 mg/day group.⁷ The decline in CRP in placebo group was not significant but in rosiglitazone group was significant ($P < 0.05$). Pfutzner A et al. showed in 2005 that a significant reduction of hs-CRP was seen after six months of therapy in pioglitazone (-0.10 ± 2.25 mg/dl, -29%, endpoint vs, baseline, $p < 0.01$) while no such change could be seen during glimepiride treatment (0.2 ± 4.0 mg/dl, -4%, $p =$ not significant).⁸ Mohanty and his colleagues reported a decrease in CRP of 30% when 11 obese patients without diabetes were treated with rosiglitazone 4 mg daily for 6 weeks.⁹

These studies are consistent with our studies regarding the reduction of serum hs-CRP level of type 2 diabetic patients by the use of thiazolidinediones. So we can conclude that thiazolidinediones can be used for type 2 diabetic patients to reduce the diabetes and its related cardiovascular complications.

In our study there was no change in high density lipoprotein (HDL) cholesterol (39 mg/dl) before and after drug in glimepiride group and 40 mg/dl before and after drug in pioglitazone group. Total cholesterol raises mildly in glimepiride group (200 mg/dl to 209 mg/dl) after treatment with glimepiride but mildly decreased in pioglitazone group after treatment with pioglitazone (211 mg/dl to 208 mg/dl). Similar mild elevation in low density lipoprotein LDL cholesterol in glimepiride group (110 mg/dl to 117 mg/dl) and mild decrease in pioglitazone group after pioglitazone intervention (115 mg/dl to 112 mg/dl). Triglyceride level was rather slightly raised in pioglitazone group after pioglitazone intervention (210 mg/dl to 212 mg/dl) and mildly reduced in glimepiride group (219 mg/dl to 216 mg/dl) (Table-III). In a word there was no significant change in lipid profile after drug intervention in our study ($p > 0.05$).

Ghazzi and his colleagues demonstrated that the troglitazone therapy decreased triglyceride level while increased high density lipoprotein (HDL) level in patients with type 2 diabetes.¹⁰ Similarly, treatment with 15, 30 and 45 mg of pioglitazone significantly decreased triglyceride compared with placebo ($P < 0.05$) and significantly increased HDL cholesterol ($P < 0.05$).¹¹ Rosiglitazone therapy also decreased triglyceride in patients with a high baseline level increased HDL cholesterol by 10% to 30%.¹²

Ours results regarding effect of pioglitazone on the lipids is not fully consistent with the above studies. This may be due to the short durations of drug application (12 weeks only) as well as use of low dose of pioglitazone (30mg), or may be due to dietary habit of our diabetic patients, because carbohydrates (rice and bread) are the main foods of our patients.

In our study population none developed pedal oedema, pulmonary oedema and congestive heart failure or became anaemic, but there was little weight gain in pioglitazone group who received pioglitazone (30 mg) for 12 weeks. There was no change in weight in glimepiride group after 12 weeks of treatment with glimepiride (Table-IV). In pioglitazone group mean increase in weight in male was 1 kg and in female it was 0.9 kg only and this increase in weight was not significant ($P > 0.05$) in comparison to glimepiride group. Haffner SM et al. showed that after 26 weeks of rosiglitazone treatment, patients in the placebo group lost 1.1 kg as opposed to 1.8 kg increase in the rosiglitazone 4 mg/day group and 3.5 kg increase in rosiglitazone 8 mg/day group ($P < 0.001$ compared with baseline). Our study is consistent with these studies.⁷

Conclusion

This small study may not reflect the exact situation of the fact in the community but its proximity to the reality can not

be underestimated. The reduction of hs-CRP level in pioglitazone group was significant in comparison to glimepiride group (0.39 mg/L Vs 0.02 mg/L). Other effects of pioglitazone, like hypoglycemic effect and effect on lipid profile were also satisfactory and no significant adverse effect was demonstrated. As diabetes is a growing epidemic globally, the morbidity and mortality of diabetes is also gradually increasing. This morbidity and mortality is mainly due to vascular complications of type-2 diabetes (stroke, myocardial infarction). It is now proved that these vascular complications, especially macrovascular complications are due to induction of chronic inflammations resulting from insulin resistance which leads to atherosclerosis. So, to prevent these incidence thiazolidinediones (pioglitazone) may be used as early pharmacological therapy in type-2 diabetic patients.

Conflict of Interest: None

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