Original Article

Efficacy of adding glutazone to the maximum dose of glibenclamide and metformin resistant on type 2 diabetic patients

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Abstract

Background: *To evaluate the efficacy of adding the glutazone to maximum dose of sulfonylurea and metformin in patients with poorly controlled type 2 diabetes.*

Methods: *Ninety six patients with type 2 diabetes who had failed medical therapy with maximal-dosage of metformin and glibenclamide received glutazone. Fasting blood sugar (FBS), 2 hours postprandial (2hpp) glucose, hemoglobin A1C, cholesterol and HDL levels were assessed at baseline three months later.*

Results: *Ninety-six patients with type 2 diabetes (74 women and 22 men) with the mean age of 55.7±9.9 years were studied. Significant reduction was seen in fasting blood sugar (FBS), 2 hours postprandial (2hpp) glucose, hemoglobin A1C and triglyceride levels three months after adding glutazone to therapeutic regimen ($p<0.0005$). There was not a significant rise in cholesterol and HDL levels before and after the new therapy.*

Conclusion: *The results show that the combination of glutazone, metformin and glibenclamide may result in better control of glycemic status in diabetic patients resistant to oral first-line agents.*

Key words: *Type 2 Diabetes, Glutazone, Metformin, Glibenclamide..*

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Type 2 diabetes mellitus is a common metabolic disorder in adults characterized by decreased insulin secretion and insulin resistance (1). Treatment is aimed at reducing blood glucose levels to normal or near-normal values. First-line monotherapy begins with sulfonylurea or metformin, and when monotherapy fails to achieve optimal glycemic control, these agents are used in combination (2). Glutazone, a member of thiazolidinedione agents, represents a new class of hypoglycemic medication which was affected by peroxisome proliferators-activated receptor-γ and has different mechanisms of action (3,4). Thiazolidinediones consistently reduce fasting and postprandial glucose concentrations as well as free fatty acid concentrations in clinical studies (5,6). The sulfonylurea acts by stimulating insulin release whereas thiazolidinediones has insulin sensitizing activity. Metformin effects on hepatic gluconeogenesis and circulating glucose levels and thereby reduced and improved peripheral insulin resistance that may also occur (7,8). Studies have shown that thiazolidinediones used as monotherapy or combination with other first-line oral agents improves glucose control (9,10).In the present clinical trial study, we evaluated the efficacy of adding glutazone to maximum dose of sulfonylurea and metformin in patients with poorly- controlled type 2 diabetes.

Methods

Ninety- six patients with type 2 diabetes referring to endocrinology clinic who had failed medical therapy including the maximum dose of metformin (1.5-2*gr*) and glibenclamide (a sulfonylurea agent) (15-20*mg*) were entered into the study.

Glutazone (15*mg) at* bedtime was added to the treatment protocol. All patients were followed up for 3 months. We assessed the glycemic status and lipid profile of the patients at the baseline and a once- a- month interval for 3 months. We also checked the liver function tests and creatinine concentration during the study period. Inclusion criteria were poorly - controlled diabetics who were resistant to primary medications.

These patients were recommended earlier to begin insulin injection therapy but all had refused to take it. Any impairment in the indicated tests prior to and throughout the study period was detected as an exclusion criteria, also patients were ineligible if they had uncontrolled hypertension, anemia, symptomatic angina, cardiac insufficiency, a body mass index greater than 40 kg/m^2 or active cancer.

Written informed consent was obtained from all the patients. An Ethics Committee of Tabriz Medical University approved the study.

Statistical analysis: The data are shown as Mean±SD. Paired t-test was used to compare the effects of glutazone on blood glucose, hemoglobin A1C and lipid profile before and after adding glutazone to therapeutic protocol. The normal distribution is measured by One-Sample Kolmogorov-Smirnov test. Statistical analyses were performed by using SPSS version 16.0. P value less than 0.05 was considered statistically significant.

Results

Ninety-six patients with type 2 diabetes (74 women and 22 men) with the mean age of 55.7±9.9 years were studied. Laboratory findings at baseline and after three months of triple therapy are shown in table 1. Significant reduction was seen in fasting blood sugar (FBS), 2 hours postprandial (2hpp) glucose levels (p<0.0005).

Glutazone significantly reduced hemoglobin A1C level three months after adding it to the previous therapeutic regimen (p<0.0005). A1C levels <7.5% were seen in 72 (75.6%) cases after 3 months. Measurement of lipid profile in patients with diabetes in a triple regimen also showed significant reduction in triglyceride level in our patients (p=0.001). There was not any significant raise in cholesterol and HDL levels with no important changes before and after the new therapy. During the study, drug intolerance or any complications due to the drug was not observed.

Table 1. The disease related characteristic before and after adding glutazone on metformin and glibenclamide

Variable (mg/dl)	Before Mean±SD	After(3month) Mean±SD	P value
FBS	215.8±43.3	142±37.7	p<0.0005
2 hpp	310±72.9	219±57.7	p<0.0005
Hb A1C%	9.2±1.4	7.2±1.3	p<0.0005
Cholesterol	182.6±46.1	189.30±65.9	0.73
TG	224.7±40.9	173.56±79.4	0.001
HDL	44.3±9.1	45.84±9.1	0.13

Discussion

The results of this study showed that in patients with type 2 diabetes receiving full dose of metformin and glibenclamide, in addition to glutazone may lead to the control of glycemic status three months after that. Hemoglobin A1C (an index of control in terms of glycemic status in diabetic patients during the past 3 months) showed a decrease after adding glutazone to the therapeutic plan when the blood sugar level was not controlled with full dose of metformin and glibenclamide protocol. Tran et al. showed that approximately two-thirds of the patients on maximal doses of metformin and a sulfonylurea agent initially responded to a maximal dose of either rosiglitazone or pioglitazone (thiazolidinediones) in 4 months after the addition of this agent (11). Other studies revealed the beneficial effects of different thiazolidinediones in combination with sulfonylurea or metformin controlled hyperglycemia in patients with type 2 diabetes which in return is similar to our findings (12-16).

Ragaglitazar compared with placebo similar to pioglitazone has shown to increase the HDL level and a reduction in cholesterol and triglyceride level in diabetic patients (17). In another study, thiazolidinedione caused a reduction in triglycerides and free fatty acids, whereas HDL cholesterol and LDL cholesterol rose slightly, with no change in apolipoprotein B (18). A significant reduction in triglyceride and cholesterol levels using pioglitazone was reported in diabetic patients (19). However in our study glutazone with combination of metformin and glibenclamide caused a reduction in triglyceride level but not in cholesterol and the HDL levels in poorly controlled diabetic patients.

In summary, the results show that the combination of glutazone, metformin and glibenclamide may result in a

better control of glycemic status in diabetic patients resistant to oral first-line agents.

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