ORIGINAL RESEARCH

Assessment of effect of rosiglitazone in type 2 diabetes with normal and abnormal liver function

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ABSTRACT

Background: Type 2 diabetes is a chronic metabolic disorder characterized by high levels of blood sugar (glucose), insulin resistance, and relative insulin deficiency. The present study was conducted to assess the effect of rosiglitazone in type 2 diabetes with normal and abnormal liver function. **Materials & Methods:**96 type 2 diabetes subjects of both genderswere divided into two groups. Group I were those with both normal serum aspartate aminotransferase and group II were subjects with either elevated serum ALT (>40 U/L) or AST (>40 U/L) level. Parameters such as fasting plasma glucose (FPG), triglyceride (TG) and total cholesterol (TC), serum high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C), serum levels of both AST and ALT and hemoglobin A1c (HbA1c) was evaluated. **Results:** group I had 28 males and 20 females and group II had 22 males and 26 females. In group I and group II, at baseline the mean BMI (Kg/m2) was 25.2and 27.9, FPG (mmol/l) was 12.5 and 10.9, TC (mmol/l) was 5.2 and 5.4, mean HDL- C (mmol/l) was 1.5 and 1.3, TG (mmol/l) was 2.6 and 2.4, AST (U/L) was 23.7 and 54.2, ALT (U/L)was 20.3 and 65.8 and HbA1C (%) was 8.6, and 8.4 respectively. The difference was significant (P< 0.05). In group I and group II, the mean BMI (Kg/m2) at 3 months was 25.0 and 27.2, FPG (mmol/l) was 11.5 and 10.1, TC (mmol/l) was 5.1 and 5.2, mean HDL- C (mmol/l) was 1.3 and 1.1, TG (mmol/l) was 2.2 and 2.1, AST (U/L) was 22.6 and 45.7, ALT (U/L) was 20.1 and 62.2 and HbA1C (%) was 8.2, and 8.0 respectively. The difference was significant (P< 0.05). **Conclusion:** A significant improvements in the levels of ALT and AST were noted in this trial following a 3-month course of rosiglitazone medication in patients with type 2 diabetes who had elevated liver enzymes.

Keywords:diabetes, liver enzymes, rosiglitazone

INTRODUCTION

Type 2 diabetes is a chronic metabolic disorder characterized by high levels of blood sugar (glucose), insulin resistance, and relative insulin deficiency. It is the most common form of diabetes, accounting for the majority of diabetes cases worldwide.[1] Unlike type 1 diabetes, which typically develops during childhood or adolescence and involves the immune system attacking the insulin-producing beta cells of the pancreas, type 2 diabetes often develops in adulthood and is associated with lifestyle factors and genetics.[2]

By associating with the peroxisome proliferation activation receptor-γ (PPAR-γ), thiazolidinedione (TZD), a kind of antidiabetic medicine, can modulate gene expression to increase insulin sensitivity.[3] It was thought to be the only medication that may help type 2 diabetics with improved insulin resistance. Regretfully, bouts of severe liver injury forced the withdrawal of the first- generation drug, troglitazone, after three years. Then, in 1999, pioglitazone and rosiglitazone of the second generation were introduced. There was no increased risk of hepatotoxicity with these medicines, according to postmarketing research.[4]There have been isolated case reports of acute hepatitis, with one death, that may be linked to rosiglitazone; however, these instances cannot completely rule out other possible causes. Therefore, the Food and Drug Administration of the United States recommended against starting rosiglitazone in patients who have moderate-to-severe liver function impairment or active liver disease.[5]The present study was conducted to assess the effect of rosiglitazone in type 2 diabetes with normal and abnormal liver function.

MATERIALS & METHODS

The present study consisted of 96 type 2 diabetes subjects of both genders. All gave their written consent to participate in the study.

Data such as name, age, gender etc. was recorded. All patients were taking rosiglitazone 4 mgdaily. The BMI was calculated as body weight/height[2] (kg/m2), while systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured. Patients were divided into two groups based on their initial liver function tests. Group I were those with both normal serum aspartate aminotransferase (AST, reference ranges £ 40 U/L) and alanine aminotransferase (ALT, reference range £ 40 U/L) levels were defined as normal liver function group (NLF) and group II were subjects with either elevated serum ALT (>40 U/L) or AST (>40 U/L) levels were defined as abnormal liver function group (ABLF). Parameters such as fasting plasma glucose (FPG), triglyceride (TG) and total cholesterol (TC), serum high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C), serum levels of both AST and ALT and hemoglobin A1c (HbA1c) was evaluated. Data thus obtained were subjected to statistical analysis. P value < 0.05 was considered significant.

RESULTS

Table I Distribution of patients

Groups	Group I	Group II
Status	NLF	ALF
M:F	28:20	22:26

Table I shows that group I had 28 males and 20 females and group II had 22 males and 26 females.

Table II Biochemical characteristics of the patients at baseline

Parameters	Group I	Group II	P value
BMI (Kg/m^2)	25.2	27.9	0.85
FPG (mmol/l)	12.5	10.9	0.04
TC (mmol/l)	5.2	5.4	0.12
HDL- C (mmol/l)	1.5	1.3	0.42
TG (mmol/l)	2.6	2.4	0.85
AST (U/L)	23.7	54.2	0.01
ALT (U/L)	20.3	65.8	0.01
HbA1C (%)	8.6	8.4	0.94

Table II, graph I shows that in group I and group II, at baseline the mean BMI (Kg/m2) was 25.2and 27.9, FPG (mmol/l) was 12.5 and 10.9, TC (mmol/l) was 5.2 and 5.4, mean HDL- C (mmol/l) was 1.5 and 1.3, TG (mmol/l) was 2.6 and 2.4, AST (U/L) was 23.7 and 54.2, ALT (U/L)was 20.3 and 65.8 and HbA1C (%) was 8.6, and 8.4 respectively. The difference was significant (P< 0.05).

Graph I Biochemical characteristics of the patients at baseline

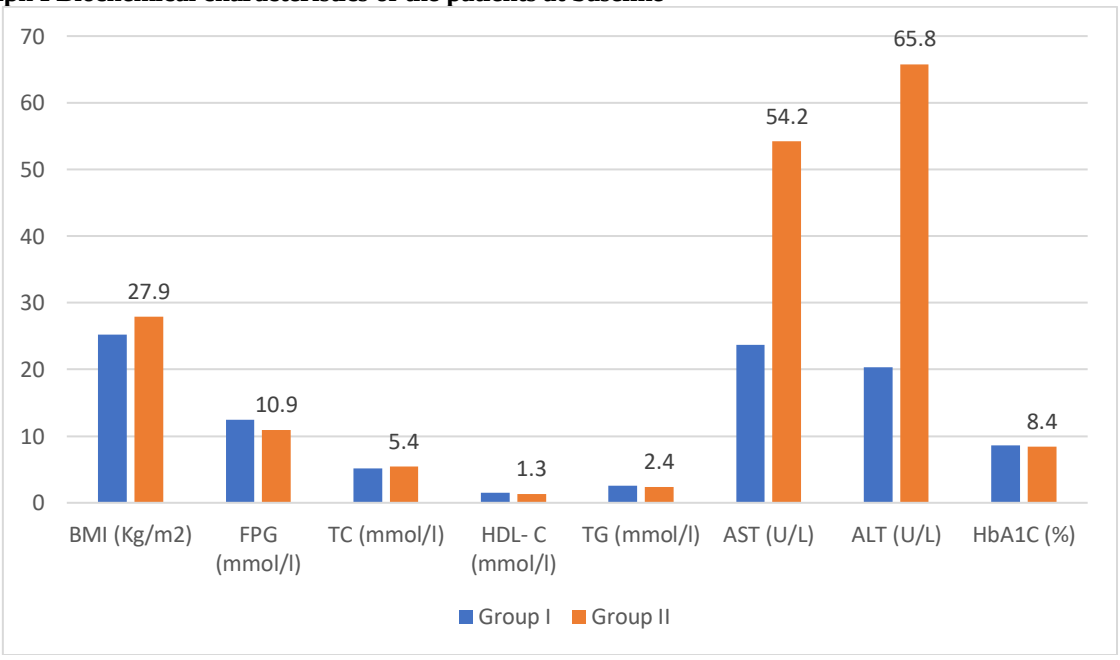

Table III Biochemical characteristics of the patients at 3 months

Parameters	Group I	Group II	P value
BMI (Kg/m^2)	25.0	27.2	0.72
FPG (mmol/l)	11.5	10.1	0.05
TC (mmol/l)	5.1	5.2	0.34
HDL- C (mmol/l)	1.3	1.0	0.49
TG (mmol/l)	2.2	2.1	0.82
AST (U/L)	22.6	45.7	0.01
ALT (U/L)	20.1	62.2	0.01
HbA1C (%)	8.2	8.0	0.42

Table III shows that in group I and group II, the mean BMI (Kg/m2)at 3 months was 25.0 and 27.2, FPG (mmol/l) was 11.5 and 10.1, TC (mmol/l) was 5.1 and 5.2, mean HDL- C (mmol/l) was 1.3 and 1.1, TG (mmol/l) was 2.2 and 2.1, AST (U/L) was 22.6 and 45.7, ALT (U/L)was 20.1 and 62.2 and HbA1C (%) was 8.2, and 8.0 respectively. The difference was significant (P< 0.05).

DISCUSSION

Cells in the body become resistant to the effects of insulin, leading to impaired glucose uptake and utilization.Family history and genetics play a significant role in the development of type 2 diabetes.[6] Certain genetic factors can increase the risk of insulin resistance and beta cell dysfunction. Excess body weight, particularly abdominal obesity, is strongly associated with insulin resistance and the development of type 2 diabetes.[7]Lack of physical activity contributes to insulin resistance and increases the risk of developing diabetes.Diets high in refined carbohydrates, sugars, and saturated fats, and low in fiber can contribute to insulin resistance and weight gain.[8]The risk of type 2 diabetes increases with age, particularly after age 45.Certain ethnic groups, including African Americans, Hispanic/Latino Americans, Native Americans, and Asian Americans, have a higher risk of developing type 2 diabetes.Women who have had gestational diabetes during pregnancy are at increased risk of developing type 2 diabetes later in life.[9,10]The present study was conducted to assess the effect of rosiglitazone in type 2 diabetes with normal and abnormal liver function.

We found that group I had 28 males and 20 females and group II had 22 males and 26 females. Zheng et al[11] in their study seventy-three patients with type 2 diabetes taking rosiglitazone 4 mg daily were enrolled in this 3-month study. Forty-two of them had normal liver function (NLF), and 31 had abnormal liver function (ABLF). Blood biochemistries were collected monthly during the treatment period.At baseline, other than age and liver enzymes, there were no differences in body mass index, fasting plasma glucose, hemoglobin A1c (HbA1c), and lipid profiles between the NLF and ABLF groups. At the end of the treatment, HbA1c was lowered in both groups, but only significantly in the ABLF group (P = 0.027). More importantly, serum concentrations of both aspartate aminotransferase (AST) and alanine aminotransferase (ALT) in the ABLF group decreased significantly (AST: 57.8 ± 26.5 to 47.5 ± 20.2 U/L, P = 0.006; ALT 66.6 ± 35.0 to 51.9 ± 23.5 UL, P = 0.004), while in the NLF group, a similar change was not found.

We found that in group I and group II, at baseline the mean BMI (Kg/m2) was 25.2and 27.9, FPG (mmol/l) was 12.5 and 10.9, TC (mmol/l) was 5.2 and 5.4, mean HDL- C (mmol/l) was 1.5 and 1.3, TG (mmol/l) was 2.6 and 2.4, AST (U/L) was 23.7 and 54.2, ALT (U/L)was 20.3 and 65.8 and HbA1C (%) was 8.6, and 8.4 respectively. We found that in group I and group II, the mean BMI (Kg/m2) at 3 months was 25.0 and 27.2, FPG (mmol/l) was 11.5 and 10.1, TC (mmol/l) was 5.1 and 5.2, mean HDL- C (mmol/l) was 1.3 and 1.1, TG (mmol/l) was 2.2 and 2.1, AST (U/L) was 22.6 and 45.7, ALT (U/L) was 20.1 and 62.2 and HbA1C (%) was 8.2, and 8.0 respectively. Rajagopalan et al[12]assessed the incidence of liver failure in association with antidiabetic treatment using pioglitazone vs. other oral antidiabetic medications. All patients, > or =18 years of age with type 2 diabetes, who had initiated treatment either with a thiazolidinedione (pioglitazone and rosiglitazone), sulfonylurea or metformin were identified and matched on the basis of propensity scores.There was no significant difference in the 1- and 2-year incidence rates of liver failure or hepatitis (primary and secondary diagnoses) between the pioglitazone monotherapy group and the respective comparator groups. In Cox proportional hazard models controlling for age, pre-index total healthcare costs, Charlson comorbidity index, procedures and a hospitalization or Emergency room (ER) visit for pre-index hyperglycaemia, and pioglitazone were not associated with an increased risk of liver failure or hepatitis, compared to all other defined groups. Furthermore, no primary or secondary diagnosis of liver failure was reported in the pioglitazone group during the follow-up period.

The limitation of the study is the small sample size.

CONCLUSION

Authors found that significant improvements in the levels of ALT and AST were noted in this trial following a 3-month course of rosiglitazone medication in patients with type 2 diabetes who had elevated liver enzymes.

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