EFFECT OF TROGLITAZONE ON URINARY ALBUMIN EXCRETION AND GLOMERULARFILTRATION RATES IN INDIVIDUALS WITH PREDIABETES

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ABSTRACT

Diabetic nephropathy is a widely accepted consequence of diabetes mellitus and is considered a leading cause for chronic kidney diseases. Prediabetes is a risk for kidney diseases since kidney damage was shown to exist prior to the development of diabetes. Increase in urinary albumin excretion is considered the earliest sign of kidney damage. Besides urinary albumin excretion rate, improvement in kidney function can also be assessed by estimating glomerular filtration rate (eGFR) form serum creatinine (SCr) levels. Data was obtained from the diabetes prevention program, a large randomized trial which evaluated the effect of troglitazone, metformin, intensive lifestyle modifications, and placebo on the prevention of diabetes mellitus. Participants were evaluated at multiple different visits including annual and at confirmation visits. This study evaluated the effect of troglitazone on preserving kidney function which was measured by its effect on estimated glomerular filtration rate (eGFR) and on urine albumin excretion rate estimated from the ratio of urine albumin-to-urine creatinine ratio (ACR). Two subgroups were selected to analyze the changes produced by troglitazone treatment from baseline visit to 12 months in eGFR values and to confirmation visit in ACR values, troglitazone effect was compared to metformin, intensive lifestyle modifications (ILS), and placebo. A total of 2,335 and 423 individuals were included in the eGFR and ACR subgroups, respectively. Troglitazone and ILS produced a statistically significant increase in eGFR (14.71 ± 3.79 and 6.86 ± 1.85, respectively, P= 0.0001). Troglitazone produced higher percentage increase in eGFR compared to lifestyle arm, 17 percent versus 10 percent (troglitazone vs. metformin: P < 0.001; troglitazone vs. lifestyle: P= 0.18; troglitazone vs. placebo: P < 0.001). Only troglitazone showed a decrease in mean ACR values from baseline to confirmation visit (-1.6 mg/gm, ±1.45, P=0.27), the rest of the interventions showed an increase, all changes did not reach a statistical significance. In conclusion, findings demonstrated the renoprotective effect of the thiazolidinedione (TZDs) presented as an increase in eGFR values and a decrease in ACR values, although the latter did not reach a statistical significance.

Keywords: Troglitazone, Metformin, Lifestyle Modification, Urinary Albumin, Prediabetes, Glomerular filtration, eGFR

INTRODUCTION

Kidney disease is a widely accepted consequence of type 2 DM; prediabetes has also emerged as a risk factor for the development of CKD (Melsom et al., 2016; & De Nicola et al., 2016). In the National Health and Nutrition Examination Survey (NHANES), the prevalence of CKD in diagnosed diabetic individuals was found to be 40 percent, while it was 18 percent in prediabetic individuals. More than 40 percent of individuals with undiagnosed diabetes or prediabetes are already affected with CKD (Snyder et al., 2009). When evaluating the extent and progression of kidney damage.

Measurement or estimation GFR measurements were proven effective in both research and clinical settings. Using hard renal evidence such as the need for renal replacement therapy, death, or doubling of serum creatinine to examine the renal protective effects is of limited benefits in clinical research since extended periods of time are generally required before any of these elements occur. The inclusion of both GFR and ACR in renal risk evaluation and classification of CKD has been considered by many investigators (Matsushita et al., 2010). Remarkable number of diabetic subjects who appear to have CDK without signs of microalbuminuria were noticed in research (Caramori et al., 2003; MacIsaac et al., 2004; Yokoyama et al., 2009; Retnakaran, Cull, & Thorne et al., 2006 & Afghahi et al., 2011). This study evaluated the effect of troglitazone as a renal protective agent, this was measured by its effect on estimated glomerular filtration rate (eGFR) and on urine albumin excretion rate estimated from the ratio of urine albumin-to-urine creatinine ratio (ACR).