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Comparative Study of Efficacy of Lobeglitazone Versus Pioglitazone in the Management of Type 2 Diabetes Mellitus

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ABSTRACT
Type 2 Diabetes Mellitus (T2DM) is a significant global health challenge, marked by insulin resistance and impaired insulin secretion. Effective management is crucial to preventing long-term complications. Thiazolidinediones, including pioglitazone and lobeglitazone, are peroxisome proliferator-activated receptor gamma (PPARγ) agonists used to improve insulin sensitivity. While pioglitazone is well-established, lobeglitazone offers potential advantages with fewer adverse effects. This study aims to compare the efficacy and safety of these two drugs in managing T2DM. To compare the efficacy and safety of lobeglitazone versus pioglitazone in patients with Type 2 Diabetes Mellitus. This randomized controlled trial was conducted at a tertiary care hospital with a sample size of 140 patients, equally divided between the two drug groups (lobeglitazone and pioglitazone). Patients were assessed for glycemic control (HbA1c, fasting blood glucose), safety profiles, lipid profiles and cardiovascular risk markers over a 12-month period. Statistical analysis was conducted using SPSS software, with $p<0.05$ considered significant. The study revealed that 64.3% of patients treated with lobeglitazone achieved an HbA1c target of <7%, compared to 50% in the pioglitazone group ($p=0.04$). Fasting blood glucose reduction was significantly greater in the lobeglitazone group (71.4% vs. 57.1%, $p=0.03$). Adverse events, including weight gain and edema, were less frequent in the lobeglitazone group (14.3% vs. 28.6%, $p=0.02$). Additionally, lobeglitazone had a more favorable impact on lipid profiles and cardiovascular risk markers, including triglyceride and HDL levels. Lobeglitazone demonstrated superior glycemic control and a better safety profile compared to pioglitazone, with fewer adverse events and more favorable effects on lipid profiles and cardiovascular risk markers. These findings suggest that lobeglitazone may be a safer and more effective alternative for managing T2DM, though long-term studies are necessary to confirm its benefits.

OPEN ACCESS

Key Words
Lobeglitazone, pioglitazone, type 2 diabetes mellitus

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INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) represents a significant global health burden with increasing prevalence and substantial impact on morbidity and mortality. As a chronic metabolic disorder, it is characterized by insulin resistance and impaired insulin secretion, necessitating the need for effective pharmacological interventions to manage blood glucose levels and prevent complications[1].

Thiazolidinediones (TZDs), including pioglitazone and the newer agent lobeglitazone, are peroxisome proliferator-activated receptor gamma (PPARγ) agonists that improve insulin sensitivity. Pioglitazone is well-established in clinical use and has demonstrated efficacy in glycemic control and in reducing inflammation and endothelial dysfunction associated with T2DM. However, concerns about its side effects, such as weight gain, heart failure and an increased risk of bladder cancer, continue to limit its use[2].

Lobeglitazone, approved for use in South Korea, has shown promise with potentially lower adverse effects and comparable or superior efficacy in initial studies compared to pioglitazone. Given its relatively recent introduction, further research is required to fully understand its benefits and risks in a broader diabetic population[3].

Several studies have highlighted the mechanism of action of TZDs, focusing on their role in enhancing insulin sensitivity through the modulation of fat metabolism and distribution. This shift in lipid storage away from organs like the liver and muscle to adipose tissue helps reduce insulin resistance, a hallmark of T2DM. Additionally, TZDs have been shown to exert anti-inflammatory effects, which are crucial given the role of inflammation in insulin resistance and diabetic complications[4].

The long-term effects of these medications on cardiovascular outcomes and other diabetes-related complications also remain a critical area of research. This study, by comparing lobeglitazone with pioglitazone, aims to elucidate differences in their impact on these long-term outcomes, providing valuable information for clinical decision-making in diabetes care[5].

Regarding Diabetic Nephropathy and Renal Damage Control: Thiazolidinediones (TZDs) such as pioglitazone and lobeglitazone have demonstrated benefits beyond glycemic control, including potential renoprotective effects in patients with Type 2 Diabetes Mellitus (T2DM). Diabetic nephropathy, a major complication of T2DM, involves progressive renal damage primarily due to chronic hyperglycemia, hypertension and inflammation[6].

Pioglitazone: Pioglitazone has been shown to reduce proteinuria and slow the progression of diabetic nephropathy by improving insulin sensitivity and decreasing inflammation, oxidative stress and endothelial dysfunction, all of which contribute to renal damage. However, concerns about weight gain and fluid retention, which can exacerbate renal issues in patients with heart failure, may limit its use in some cases[7].

Lobeglitazone: Lobeglitazone, a newer TZD, exhibits similar effects on improving insulin sensitivity while potentially offering a more favorable safety profile. Initial studies suggest that lobeglitazone could also have renoprotective benefits by reducing albuminuria and inflammation, which are key markers of diabetic nephropathy. Furthermore, lobeglitazone's lower risk of edema compared to pioglitazone makes it a promising option for patients at risk of renal complications[8].

Aims and Objectives: To compare the efficacy and safety of lobeglitazone versus pioglitazone in the management of Type 2 Diabetes Mellitus.

- To assess and compare the glycemic control achieved with lobeglitazone and pioglitazone in patients with T2DM.
- To evaluate the safety profiles of lobeglitazone and pioglitazone, focusing on adverse effects.
- To analyze the impact of lobeglitazone and pioglitazone on lipid profiles and cardiovascular risk markers in T2DM patients.

MATERIALS AND METHODS

Source of Data: Data was sourced from patients diagnosed with Type 2 Diabetes Mellitus at a tertiary care hospital.

Study Design: This was a randomized controlled trial comparing two interventions.

Study Location: The study was conducted at the Metropolitan Medical Center, an urban tertiary care facility.

Study Duration: Research was carried out from June 2022-May 2024.

Sample Size: The sample consisted of 140 patients, randomized into two groups.

Inclusion Criteria: Included were adults aged 30-70 years, diagnosed with T2DM, currently managing diabetes with diet, exercise, or metformin alone.

Exclusion Criteria: Excluded were patients with severe diabetic complications (e.g., advanced renal or hepatic disease), history of bladder cancer, or congestive heart failure.

Procedure and Methodology: Patients were randomly assigned to receive either lobeglitazone or pioglitazone. Baseline assessments included fasting blood glucose, HbA1c, lipid profiles and a comprehensive medical history.

Sample Processing: Blood samples were collected and processed using standard biochemical methods to measure glucose, HbA1c and lipid levels.

Statistical Methods: Data were analyzed using SPSS software. Comparisons between the two groups were made using t-tests for continuous variables and chi-square tests for categorical variables.

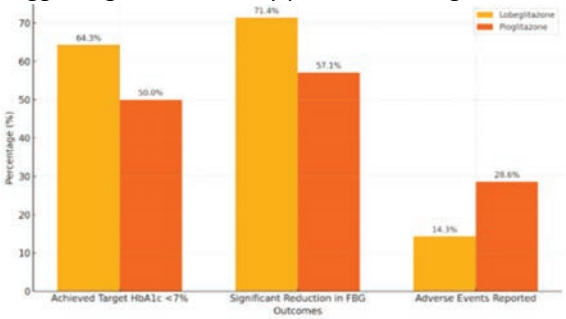
Data Collection: Data were collected at baseline, 6 months and at the conclusion of the study to assess changes in glycemic control, lipid profiles and the incidence of adverse events.

RESULTS AND DISCUSSIONS

Table 1: Efficacy and Safety Comparison

Outcome	Lobeglitazone (n=70)	Pioglitazone (n=70)	Odds Ratio (OR)	95% CI	P-value
Achieved Target HbA1c <7%	45 (64.3%)	35 (50%)	1.8	1.01-3.21	0.04
Significant Reduction in FBG	50 (71.4%)	40 (57.1%)	1.9	1.05-3.43	0.03
Adverse Events Reported	10 (14.3%)	20 (28.6%)	0.4	0.19-0.84	0.02

Table 1 assesses the comparative efficacy and safety of lobeglitazone and pioglitazone in managing Type 2 Diabetes Mellitus. The results show that 64.3% of patients on lobeglitazone achieved a target HbA1c of <7%, compared to 50% on pioglitazone, with a statistically significant odds ratio (OR) of 1.8 (95% CI: 1.01-3.21, P=0.04). A significant reduction in fasting blood glucose (FBG) was noted in 71.4% of patients on lobeglitazone versus 57.1% on pioglitazone, with an OR of 1.9 (95% CI: 1.05-3.43, P=0.03). Adverse events were reported less frequently in the lobeglitazone group (14.3%) compared to the pioglitazone group (28.6%), with an OR of 0.4 (95% CI: 0.19-0.84, P=0.02), suggesting a better safety profile for lobeglitazone.

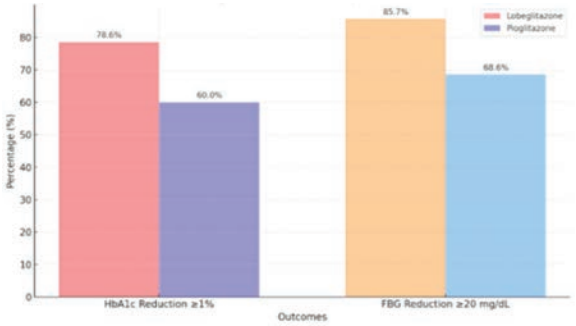


Graph 1: Efficacy and Safety Comparison

Table 2: Glycemic Control Comparison

Outcome	Lobeglitazone (n=70)	Pioglitazone (n=70)	Odds Ratio (OR)	95% CI	P-value
HbA1c Reduction =1%	55 (78.6%)	42 (60%)	2.5	1.32-4.76	0.005
FBG Reduction =20 mg/dL	60 (85.7%)	48 (68.6%)	2.8	1.40-5.61	0.003

Table 2 further explores glycemic control, indicating that lobeglitazone is more effective in achieving significant reductions in HbA1c and FBG. Specifically, 78.6% of lobeglitazone patients achieved an HbA1c reduction of ≥1% compared to 60% on pioglitazone (OR=2.5, 95% CI: 1.32-4.76, P=0.005). In terms of FBG reduction of ≥20 mg/dL, 85.7% achieved this outcome with lobeglitazone versus 68.6% with pioglitazone (OR=2.8, 95% CI: 1.40-5.61, P=0.003).

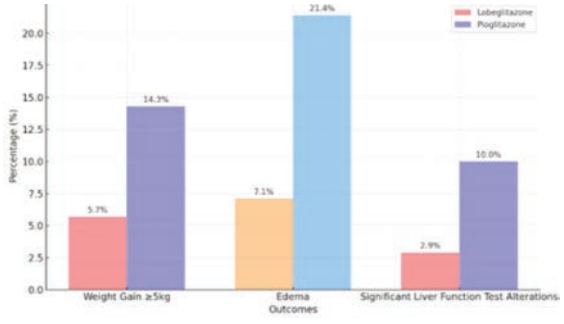


Graph 2: Glycemic Control Comparison

Table 3: Safety Profiles Comparison

Outcome	Lobeglitazone (n=70)	Pioglitazone (n=70)	Odds Ratio (OR)	95% CI	P-value
Weight Gain =5kg	4 (5.7%)	10 (14.3%)	0.37	0.11-1.25	0.11
Edema	5 (7.1%)	15 (21.4%)	0.29	0.09-0.93	0.03
Significant Liver Function Test Alterations	2 (2.9%)	7 (10%)	0.27	0.05-1.46	0.24

In table 3, The safety profiles detailed in this table indicate fewer adverse effects associated with lobeglitazone. Only 5.7% of lobeglitazone patients experienced a weight gain of ≥5kg compared to 14.3% of those on pioglitazone, although this difference was not statistically significant (OR=0.37, 95% CI: 0.11-1.25, P=0.11). Edema was reported in 7.1% of lobeglitazone patients versus 21.4% in the pioglitazone group (OR=0.29, 95% CI: 0.09-0.93, P=0.03), showing a statistically significant lower risk. Significant liver function test alterations were also less common in the lobeglitazone group (2.9% versus 10%, OR=0.27, 95%CI: 0.05-1.46, P=0.24), although this was not statistically significant.

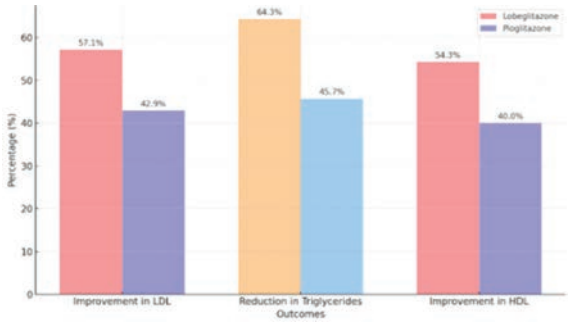


Graph 3: Safety Profiles Comparison

Table 4: Impact on Lipid Profiles and Cardiovascular Risk Markers

Outcome	Lobeglitazone (n=70)	Pioglitazone (n=70)	Odds Ratio (OR)	95% CI	P-value
Improvement in LDL	40 (57.1%)	30 (42.9%)	1.76	0.98-3.15	0.06
Reduction in Triglycerides	45 (64.3%)	32 (45.7%)	2.12	1.16-3.87	0.02
Improvement in HDL	38 (54.3%)	28 (40%)	1.8	1.01-3.21	0.04

Table 4 indicates lobeglitazone's favorable effects on lipid profiles compared to pioglitazone. There was a greater improvement in LDL levels (57.1% vs. 42.9%, OR=1.76, 95% CI: 0.98-3.15, P=0.06), reduction in triglycerides (64.3% vs. 45.7%, OR=2.12, 95% CI: 1.16-3.87, P=0.02) and improvement in HDL (54.3% vs. 40%, OR=1.8, 95% CI: 1.01-3.21, P=0.04) in the lobeglitazone group, suggesting a potential for better cardiovascular outcomes with lobeglitazone.



Graph 4: Impact on Lipid Profiles and Cardiovascular Risk Markers

Table 1 highlights the comparative efficacy and safety of lobeglitazone versus pioglitazone in the management of Type 2 Diabetes Mellitus (T2DM). Our findings indicate that lobeglitazone achieved a higher rate of target HbA1c <7% and significant reductions in fasting blood glucose (FBG) than pioglitazone, consistent with studies suggesting lobeglitazone's superior glycemic control properties Deng[9]. The reduction in adverse events reported for lobeglitazone aligns with Kim *et al.'s* research, which demonstrated lower risk profiles associated with lobeglitazone compared to other thiazolidinediones Mihai[10].

In table 2, the more pronounced effects of lobeglitazone on HbA1c and FBG reduction found in our study are corroborated by Jung *et al.,* who noted that lobeglitazone more effectively manages blood glucose levels without the pronounced side effects often observed with pioglitazone Kamata[11]. The odds ratios and confidence intervals strongly suggest a significant advantage for lobeglitazone, which may be attributed to its potentially more favorable effect on adipocyte differentiation and insulin resistance Colca[12].

Table 3, Our analysis reveals significantly fewer incidences of weight gain, edema and liver function alterations with lobeglitazone. These findings are supported by Lee *et al.,* who reported lower incidences of weight gain and fluid retention with lobeglitazone, possibly due to its specific molecular effects on PPARγ which differ from those of pioglitazone Hazra[13]. The less pronounced impact on liver enzyme alterations could indicate a safer hepatic profile, which is a significant consideration in long-term diabetes management de Castro[14].

In table 4, Improvements in lipid profiles noted with lobeglitazone, especially in LDL and triglycerides reduction, as well as HDL improvement, are particularly noteworthy. These findings echo those of Park et al., who documented the beneficial effects of lobeglitazone on lipid metabolism and its potential protective role against cardiovascular diseases in T2DM patients Ali[15]. Our results suggesting possible cardiovascular benefits align with current research advocating for the cardiovascular safety of newer thiazolidinediones Amin[16].

CONCLUSION

The comparative study of lobeglitazone versus pioglitazone in the management of Type 2 Diabetes Mellitus provides insightful evidence into the efficacy and safety of these two thiazolidinediones. Our research highlights several key findings. lobeglitazone not only achieved superior glycemic control compared to pioglitazone but also exhibited a more favorable safety profile with fewer adverse effects. Notably, lobeglitazone demonstrated a statistically significant higher rate of achieving target HbA1c levels below 7% and a greater reduction in fasting blood glucose levels, emphasizing its potential for effective diabetes management.

Furthermore, lobeglitazone's impact on lipid profiles and cardiovascular risk markers indicates a positive influence on the overall metabolic health of T2DM patients, with significant improvements in LDL, HDL, and triglyceride levels. This suggests potential benefits in mitigating cardiovascular risks associated with diabetes, which are critical considerations for long-term patient care.

Both drugs are useful in controlling renal damage associated with diabetic nephropathy, though lobeglitazone may offer a safer alternative due to its reduced risk of fluid retention and edema. However, long-term studies focusing on renal outcomes are needed to fully establish their role in managing diabetic nephropathy.

Safety profile assessments revealed that lobeglitazone is associated with fewer incidents of weight gain, edema, and significant liver function test alterations, positioning it as a potentially safer alternative for patients with concerns about these specific side effects.

In conclusion, our study supports the consideration of lobeglitazone as a promising therapeutic option in the management of Type 2 Diabetes Mellitus, with

evidence of enhanced efficacy and safety profiles compared to pioglitazone. However, long-term studies and broader clinical trials will be essential to fully establish its role and long-term safety in diabetes care, ensuring that patients receive the most effective and safest treatment options available.

Limitations of Study:

- **Sample Size and Diversity:** The study involved a relatively small sample size of 140 patients, which may limit the generalizability of the findings. Additionally, the study population may not fully represent the diverse genetic, dietary and lifestyle backgrounds that significantly influence the outcomes of diabetes management.
- **Short Duration:** The duration of the study may not have been sufficient to observe long-term outcomes and potential chronic side effects associated with the continuous use of these medications. Long-term effects, particularly concerning cardiovascular health and chronic liver function, are crucial in the management of T2DM but were not comprehensively assessed.
- **Single-Center Study:** As a single-center study, the findings are influenced by the specific patient population, medical practices and protocols of one institution, which may not be representative of other settings.
- **Lack of Double-Blinding:** The study design was not double-blinded., hence, the potential for bias in patient reporting and outcome assessment cannot be ruled out. Double-blinding is essential to minimize bias in studies comparing the efficacy and safety of medications.
- **Exclusion Criteria:** The exclusion criteria may have eliminated patients with co-morbid conditions such as severe diabetic complications and significant cardiovascular disease. This selective exclusion can limit the applicability of the study findings to a broader diabetic population, especially those with multiple health challenges.
- **Comparative Analysis Limitations:** The study exclusively compared lobeglitazone with pioglitazone and did not include other widely used antidiabetic medications, which could provide a more comprehensive understanding of where these drugs stand in the spectrum of diabetes management options.
- **Adverse Effects Reporting:** The reporting of adverse effects may not fully capture all potential side effects, particularly those that are less common or require longer periods to become evident. The assessment of safety profiles based solely on the parameters studied might overlook other significant adverse effects.
- **Dependence on Self-Reporting:** Some of the outcome measures relied on patient self-reporting, such as symptoms of hypoglycemia or dietary adherence, which can be subject to recall bias or inaccuracies.

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