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Original Research Article

Clinical Evaluation of Pioglitazone's Impact on Insulin Resistance and Blood Pressure in Type 2 Diabetic Patients Undergoing Hemodialysis

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Abstract:

Background: Globally, type 2 diabetes mellitus (T2DM) is becoming more common, especially in individuals receiving hemodialysis for end-stage renal disease (ESRD). This population faces heightened risks of cardiovascular complications and poor glycemic control. Pioglitazone, an insulin sensitizer, has shown potential in improving metabolic and cardiovascular parameters but its application in hemodialysis patients remains underexplored.

Aim: To assess the impact of pioglitazone on blood pressure, glycemic management, and insulin resistance in patients with type 2 diabetes receiving hemodialysis.

Methods: This prospective observational study included 100 type 2 diabetic patients on maintenance hemodialysis. Participants were administered pioglitazone (15–30 mg daily) for six months. Baseline and follow-up parameters including HbA1c, fasting insulin, HOMA-IR (Homeostasis Model Assessment of Insulin Resistance), and blood pressure were measured. Statistical analyses were performed using SPSS version 23.0, with paired t-tests and Chi-square tests to assess pre- and post-treatment differences.

Results: Significant improvements were observed post-treatment: HbA1c decreased from 8.5 ± 1.2% to 7.3 ± 1.0% ($p < 0.001$), fasting insulin levels reduced from 24.8 ± 6.5 µIU/mL to 17.5 ± 4.8 µIU/mL ($p < 0.001$), and HOMA-IR declined from 5.8 ± 1.4 to 3.4 ± 0.8 ($p < 0.001$). Systolic and diastolic blood pressure decreased by 11.7 mmHg and 6.1 mmHg, respectively ($p < 0.001$). 85% of participants showed improvement, 10% had no change, and 5% reported mild adverse effects.

Conclusion: Pioglitazone significantly improved insulin resistance, glycemic control, and blood pressure in type 2 diabetic patients on hemodialysis, with minimal adverse effects.

Recommendations: Further large-scale, randomized controlled trials are recommended to establish long-term safety and efficacy of pioglitazone in this patient population. Routine monitoring for potential side effects is advised when using pioglitazone in clinical practice.

Keywords: Pioglitazone, Type 2 Diabetes Mellitus, Hemodialysis, Insulin Resistance, Cardiovascular Risk

Introduction

Insulin resistance and β-cell malfunction cause chronic hyperglycemia, which is a common metabolic condition known as (T2DM). The global rise in T2DM cases has led to increased morbidity and mortality, particularly from cardiovascular complications. Among T2DM patients, those undergoing hemodialysis for (ESRD)

face compounded health challenges, including heightened cardiovascular risk and complex glycemic management [1,2].

By activating peroxisome proliferator-activated receptor-gamma (PPAR-γ), pioglitazone, a thiazolidinedione, improves glucose absorption in peripheral tissues and increases insulin sensitivity. Pioglitazone has been shown to have cardiovascular advantages in addition to glycemic control. In those with insulin resistance and prediabetes, pioglitazone medication was linked to a lower incidence of major adverse cardiovascular events (MACE), according to a 2019 meta-analysis, underscoring its promise in lowering cardiovascular risk [3].

Managing T2DM in hemodialysis patients is particularly challenging due to altered pharmacokinetics and increased susceptibility to adverse drug effects. Traditional antidiabetic medications often require dose adjustments or are contraindicated in ESRD. Pioglitazone, primarily metabolized hepatically, offers a therapeutic advantage in this context. However, concerns about fluid retention and heart failure have limited its use. Recent studies have sought to evaluate the safety and efficacy of pioglitazone in this population. Pioglitazone may be beneficial in this high-risk population, as evidenced by a 2020 study that revealed its usage in T2DM patients with ESRD was linked to fewer (MACCEs) and mortality when compared to other antidiabetic medications [4].

Despite these findings, the application of pioglitazone in hemodialysis patients remains limited. A 2021 review emphasized the need for individualized treatment strategies in T2DM patients with chronic kidney disease, noting that while pioglitazone may offer benefits, careful patient selection and monitoring are essential to mitigate risks [5]. Additionally, low-dose pioglitazone was shown to be safe and efficacious in T2DM patients with chronic renal disease, minimizing side effects while preserving therapeutic efficacy in a randomized controlled trial [6].

In conclusion, pioglitazone presents a promising option for improving insulin sensitivity and potentially reducing cardiovascular events in T2DM patients undergoing hemodialysis. Its unique pharmacological profile makes it suitable for this population, but concerns about adverse effects necessitate cautious use. Further large-scale, randomized controlled trials are needed to establish definitive safety and efficacy profiles for pioglitazone in hemodialysis patients, guiding clinicians in optimizing treatment strategies for this vulnerable group [6]. To assess the impact of pioglitazone on blood pressure, glycemic management, and insulin resistance in patients with type 2 diabetes receiving hemodialysis.

Methodology

Study Design

This study is an observational prospective study.

Study Setting

The study will be carried out at the nephrology department of a tertiary care hospital. The study will be conducted over a period of 12 months.

Participants

The trial will include 100 patients with type 2 diabetes who get regular hemodialysis. Specific inclusion and exclusion criteria will be used to choose participants in order to guarantee the validity of the findings.

Inclusion Criteria:

- People with a verified diagnosis of type 2 diabetes mellitus who are between the ages of 30 and 70.
- Individuals receiving hemodialysis for maintenance for a minimum of six months.
- Individuals who have maintained stable blood pressure and glucose control for the last three months.

- The ability to give written, informed consent.

Exclusion Criteria:

- Patients with T1DM.
- Those with severe cardiovascular complications or active infections.
- Patients using other insulin-sensitizing agents or antihypertensive drugs within the last 3 months.
- Pregnant or lactating women.

Bias

To minimize selection bias, random sampling methods will be used to enroll participants. Additionally, confounding variables such as baseline blood pressure, glycemic status, and comorbidities will be statistically adjusted during analysis to avoid bias.

Data Collection

Reviewing medical records, interviewing patients, and conducting laboratory tests will all be used to gather data. HOMA-IR (Homeostasis Model Assessment of Insulin Resistance), fasting insulin, blood pressure, and HbA1c are baseline measurements that will be taken prior to starting pioglitazone therapy. Following the start of treatment, follow-up information will be gathered at one, three, and six months.

Procedure

After obtaining informed consent, participants will be administered pioglitazone at a standard dose of 15–30 mg daily, as per clinical guidelines. Patients will continue their regular hemodialysis schedule, and any adverse effects or changes in clinical status will be closely monitored. At every follow-up, the impact of pioglitazone on blood pressure and insulin resistance will be evaluated.

Statistical Analysis

SPSS version 23.0 will be used to analyze the data. Categorical variables will be represented as percentages, and continuous variables as mean ± standard deviation (SD). Values before and after treatment will be compared using paired t-tests. We'll use chi-square testing for categorical results. We'll use multivariate regression analysis to account for possible confounders. Statistical significance will be established when the p-value is less than 0.05.

Results

Out of 100 participants, the mean age was 56.4 ± 8.2 years, with 60% being male and 40% female. The average duration of diabetes was 10.5 ± 3.2 years, and the mean duration of hemodialysis was 24.3 ± 6.7 months. This distribution ensured a representative sample for the study.

Table 1: Participant Demographics and Baseline Characteristics

Characteristic	Mean ± SD or Count (%)
Age (years)	56.4 ± 8.2
Gender (Male/Female)	60/40
Duration of Diabetes (years)	10.5 ± 3.2
Hemodialysis Duration (months)	24.3 ± 6.7

Changes in Clinical Parameters

Significant improvements were observed in glycemic control, insulin resistance, and blood pressure post-treatment with pioglitazone.

Table 2: Changes in Clinical Parameters

Parameter	Baseline Mean ± SD	Post-Treatment Mean ± SD	Mean Difference	p-Value
HbA1c (%)	8.5 ± 1.2	7.3 ± 1.0	-1.2	<0.001
Fasting Insulin (μIU/mL)	24.8 ± 6.5	17.5 ± 4.8	-7.3	<0.001
HOMA-IR	5.8 ± 1.4	3.4 ± 0.8	-2.4	<0.001
Systolic BP (mmHg)	148.2 ± 12.6	136.5 ± 10.2	-11.7	<0.001
Diastolic BP (mmHg)	88.4 ± 8.5	82.3 ± 6.9	-6.1	<0.001

Response Rate

- **85%** showed significant improvement in glycemic and blood pressure parameters.
- **10%** exhibited no improvement.
- **5%** reported minor adverse events such as mild edema.

Table 3: Response Rate

Response	Count	Percentage (%)
Improved	85	85
No Improvement	10	10
Adverse Events	5	5

The results demonstrate a statistically significant improvement in all evaluated parameters:

- **HbA1c levels** reduced significantly, reflecting improved glycemic control.
- **Fasting insulin levels** and **HOMA-IR** showed marked reductions, indicating enhanced insulin sensitivity.
- **Blood pressure** improvements were consistent, with both systolic and diastolic pressures significantly decreasing.

Discussion

A total of 100 participants, with a mean age of 56.4 years and an average diabetes duration of 10.5 years, were enrolled. The balanced gender distribution (60% male, 40% female) and the mean hemodialysis duration of 24.3 months ensured a representative cohort for evaluating the effects of pioglitazone.

Post-treatment analysis revealed significant improvements in key parameters. HbA1c levels decreased from 8.5 ± 1.2% at baseline to 7.3 ± 1.0%, indicating enhanced glycemic control ($p < 0.001$). Similarly, fasting insulin levels reduced from 24.8 ± 6.5 μIU/mL to 17.5 ± 4.8 μIU/mL, and HOMA-IR values declined from 5.8 ± 1.4 to 3.4 ± 0.8, reflecting a substantial improvement in insulin sensitivity ($p < 0.001$ for both). These findings suggest that pioglitazone effectively targets the underlying insulin resistance in this patient population.

Blood pressure outcomes were equally encouraging. Systolic blood pressure decreased by 11.7 mmHg (148.2 ± 12.6 mmHg to 136.5 ± 10.2 mmHg), and diastolic blood pressure reduced by 6.1 mmHg (88.4 ± 8.5 mmHg to 82.3 ± 6.9 mmHg), both showing statistical significance ($p < 0.001$). These reductions are clinically meaningful and may contribute to reducing cardiovascular risk in patients with diabetes and chronic kidney disease.

The response rate analysis showed that 85% of participants experienced significant

improvement in glycemic and blood pressure parameters, 10% exhibited no improvement, and 5% reported mild adverse events such as edema. The minimal adverse effects highlight the safety and tolerability of pioglitazone in this population.

Pioglitazone has demonstrated substantial benefits in improving insulin sensitivity, metabolic profiles, and cardiovascular health among diabetic and insulin-resistant populations. A systematic review and meta-analysis confirmed that pioglitazone monotherapy effectively reduces fasting blood sugar levels, improves insulin sensitivity (as measured by HOMA-IR), and ameliorates adverse lipid profiles and blood pressure. However, it is associated with weight gain and increased risk of edema, which necessitates careful patient selection for therapy [7]. Another study from the IRIS trial showed that pioglitazone significantly reduced the risk of ischemic stroke in insulin-resistant patients following a transient ischemic attack or prior stroke. This highlights its potential for secondary prevention of cerebrovascular events [8].

A study investigating the combination therapy of pioglitazone and metformin revealed superior reductions in insulin resistance and lipid profiles compared to pioglitazone alone, with no significant increase in adverse events, demonstrating the clinical potential of combination regimens [9]. Pioglitazone also improved (NAFLD) in type 2 diabetic patients. This improvement was seen in liver steatosis, insulin resistance, and inflammation, even at low doses, and was independent of glucose control [10].

In hemodialysis patients, a randomized controlled trial found that pioglitazone significantly enhanced protein metabolism and reduced markers of chronic inflammation, suggesting its utility in mitigating protein energy wasting in this high-risk population [11]. Furthermore, pioglitazone was found to regulate adipose tissue-specific miRNA and extracellular vesicle-mediated pathways, which contributed to improved systemic insulin sensitivity and interorgan metabolic regulation [12].

Conclusion

This study shows that pioglitazone effectively improves glycemic control, insulin resistance, and blood pressure in type 2 diabetic patients undergoing hemodialysis. Reductions in HbA1c, fasting insulin, HOMA-IR, and blood pressure underscore its potential in managing metabolic and cardiovascular risks. Minimal adverse effects support its safety, suggesting it could be a valuable therapy for insulin resistance and hypertension in end-stage renal disease. Further large-scale, long-term studies are needed to confirm these benefits and assess potential risks.

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