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Original Research Article

GLYCEMIC CONTROL AND CARDIOVASCULAR RISK IN PATIENTS ON DUAL THERAPY WITH METFORMIN AND ACE INHIBITORS: A LONGITUDINAL OBSERVATIONAL STUDY

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Abstract

Background: Type 2 Diabetes Mellitus carries an elevated risk of cardiovascular complications. Metformin and ACE Inhibitors, a common dual therapy, are used in diabetes management. This observational study assessed the impact of Metformin and ACE Inhibitors on key parameters in 100 Type 2 Diabetes patients. **Materials and Methods:** A diverse group of 100 patients, composed of 55 males and 45 females, with an average age of 55.4 ± 6.9 years, participated in this study. The primary outcome measures encompassed glycemic control, indicated by HbA1c levels, blood pressure, lipid profiles (Total Cholesterol, LDL Cholesterol, HDL Cholesterol, and Triglycerides), and the incidence of cardiovascular events. These parameters were assessed at baseline and following 6 and 12 months of dual therapy. **Result:** Over the study period, glycemic control improved significantly, as reflected by HbA1c levels decreasing from 8.2% at baseline to 7.1% at 12 months ($p < 0.01$). Both systolic and diastolic blood pressure exhibited marked reductions, declining from 142.6/89.2 mmHg at baseline to 128.1/80.9 mmHg at 12 months ($p < 0.01$). Unexpectedly, lipid profile components showed no statistically significant changes over the 12-month period. During the 12-month follow-up, only one incident each of myocardial infarction and stroke were observed, and these events did not significantly deviate from the expected rate in this patient cohort. **Conclusion:** Metformin and ACE Inhibitors effectively improved glycemic control and lowered blood pressure in Type 2 Diabetes patients. However, lipid profiles remained unchanged, suggesting limited impact on cardiovascular risk. The low incidence of cardiovascular events warrants further investigation with larger cohorts and extended follow-up to clarify this therapy's role in reducing cardiovascular risk in this population.

INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is a pervasive and chronic metabolic disorder characterized by elevated blood glucose levels, primarily resulting from insulin resistance and insufficient insulin production.[1] It represents a significant global health challenge due to its rising prevalence, associated complications, and healthcare burdens.[2] A particularly concerning aspect of T2DM is its strong association with cardiovascular diseases (CVD), which include conditions such as coronary artery disease, stroke, and heart failure.[3] These cardiovascular complications are a leading cause of morbidity and mortality among individuals with diabetes.[4]

To mitigate the increased cardiovascular risk in T2DM patients, therapeutic approaches go beyond glycemic control alone. Dual therapy involving Metformin, an oral hypoglycemic agent, and Angiotensin-Converting Enzyme (ACE) Inhibitors, commonly prescribed for hypertension and cardiac conditions, has gained prominence in diabetes management. The rationale behind this dual therapy lies in its potential to address not only glycemic control but also cardiovascular risk factors, including hypertension and lipid profiles.

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Rationale and Significance

The significance of investigating the impact of Metformin and ACE Inhibitors dual therapy in T2DM patients is multifaceted. First and foremost, T2DM is escalating globally, with the International Diabetes Federation (IDF) estimating that over 500 million people will be affected by 2045. The accompanying cardiovascular risk amplifies the urgency of effective treatment strategies. Dual therapy is an attractive option as it combines agents with complementary mechanisms of action, potentially offering comprehensive cardiovascular protection.

Secondly, the association between glycemic control, blood pressure, lipid profiles, and cardiovascular events is intricate. While glycemic control is a pivotal aspect of diabetes management, blood pressure and lipid profiles are equally vital determinants of cardiovascular risk. Thus, examining how this dual therapy influences these parameters and their interplay is crucial for optimizing patient care.

Aim and Objectives

The primary aim of this longitudinal observational study is to comprehensively assess the effects of dual therapy with Metformin and ACE Inhibitors on key parameters in a cohort of 100 Type 2 Diabetes patients. To achieve this aim, the study has the following specific objectives:

Evaluate Glycemic Control: To measure the impact of dual therapy on glycemic control as indicated by changes in HbA1c levels over 12 months.

Assess Blood Pressure Regulation: To determine how dual therapy influences systolic and diastolic blood pressure and whether it leads to significant reductions.

Examine Lipid Profile Changes: To investigate whether dual therapy affects lipid profile components, including Total Cholesterol, LDL Cholesterol, HDL Cholesterol, and Triglycerides, over the study period.

Analyze Cardiovascular Events: To assess the incidence of cardiovascular events, such as myocardial infarction and stroke, during the 12-month follow-up and compare it to the expected rate in this patient cohort.

MATERIALS AND METHODS

This comprehensive longitudinal observational study aimed to investigate the effects of dual therapy with Metformin and Angiotensin-Converting Enzyme (ACE) Inhibitors on glycemic control, blood pressure, lipid profiles, and cardiovascular events within a cohort of 100 Type 2 Diabetes Mellitus (T2DM) patients. The study adhered to rigorous ethical guidelines and received approval from the institutional review board. It was conducted at Andhra Medical College, Vishakhapatnam, spanning from April 2022 to March 2023.

Study Design: In this longitudinal observational study, the focus was on examining the trajectories and contributing factors of Type 2 Diabetes Mellitus. Spanning a 12-month period from April 2022 to March 2023, the research involved a cohort of 100 participants, all of whom had received a diagnosis of Type 2 Diabetes Mellitus. Stringent inclusion and exclusion criteria were employed to curate a participant pool that was both diverse and directly relevant to the research goals.

Inclusion Criteria

- Adults aged 18 years and above.
- Confirmed diagnosis of Type 2 Diabetes Mellitus.
- Prescribed dual therapy with Metformin and ACE Inhibitors.

Exclusion Criteria

- Patients with contraindications to Metformin or ACE Inhibitors.
- Individuals concurrently taking other diabetes medications.
- Participants with a documented history of adverse reactions to Metformin or ACE Inhibitors.

Data Collection

Demographic Data: Patient demographics, including age, gender, and relevant medical history, were meticulously recorded.

Baseline Measurements: Baseline assessments included critical parameters such as glycemic control (HbA1c levels), blood pressure (both systolic and diastolic readings), and lipid profiles (comprising Total Cholesterol, LDL Cholesterol, HDL Cholesterol, and Triglycerides).

Follow-up Visits: Study participants were closely monitored at two subsequent time points: 6 months and 12 months post-initiation of dual therapy.

Cardiovascular Events: The study systematically documented and tracked any incidences of cardiovascular events, such as myocardial infarction and stroke, throughout the 12-month follow-up period.

Intervention: Study participants received dual therapy consisting of Metformin and ACE Inhibitors, as prescribed by their treating physicians. Medication compliance was meticulously monitored during follow-up visits to ensure adherence to the prescribed regimen.

Outcome Measures: Glycemic Control: HbA1c levels were assessed at baseline and subsequently at the 6-month and 12-month follow-up visits.

Blood Pressure: Systolic and diastolic blood pressure measurements were recorded during each assessment, enabling the tracking of changes over time.

Lipid Profiles: The study meticulously evaluated lipid profile components, including Total Cholesterol, LDL Cholesterol, HDL Cholesterol, and Triglycerides, at baseline, 6 months, and 12 months.

Cardiovascular Events: Incidences of cardiovascular events, specifically myocardial infarction and stroke, were closely monitored and recorded during the entire 12-month follow-up period.

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Statistical Analysis: Descriptive statistics were employed to concisely summarize demographic data and the key parameters under investigation.

Changes in HbA1c levels, blood pressure readings, and lipid profile components over the study's duration were meticulously analyzed using paired t-tests to identify statistically significant trends.

The incidence of cardiovascular events was reported and meticulously compared to the expected rates to ascertain any significant deviations or trends.

Ethical Considerations: The study was conducted in strict adherence to established ethical guidelines to safeguard patient rights, privacy, and confidentiality. Prior to any data collection or participation in the study, informed consent was obtained from all study participants. The study received formal approval from the institutional review board before commencement, ensuring ethical integrity throughout the research process.

RESULTS

The study presents a longitudinal observational analysis of 100 patients, all diagnosed with Type 2 Diabetes Mellitus, undergoing dual therapy with Metformin and ACE Inhibitors. The purpose is to evaluate the effects of this treatment on glycemic control, blood pressure, lipid profile, and the incidence of cardiovascular events.

Demographics: The patient cohort included 55 males and 45 females, averaging 55.4 ± 6.9 years in age. This is a balanced gender distribution and the age range is representative of a middle-aged population often affected by Type 2 Diabetes.

Glycemic Control: Measured by HbA1c levels, glycemic control improved over the course of the study. The mean HbA1c levels reduced from 8.2% at the baseline to 7.1% at 12 months. The p-values indicate that these reductions were statistically significant. Thus, dual therapy appears effective in controlling blood sugar levels.

Blood Pressure: Both systolic and diastolic blood pressure showed statistically significant reductions during the study. Starting from a mean of 142.6/89.2 mmHg, they reduced to 128.1/80.9 mmHg at 12 months. This is crucial as high blood pressure is a known cardiovascular risk factor, especially in diabetic patients.

Lipid Profile: Interestingly, the study did not find any significant changes in the lipid profile components (Total Cholesterol, LDL Cholesterol, HDL Cholesterol, and Triglycerides) over the 12-month period. The p-values were all above 0.05, indicating that any change observed was not statistically significant.

Cardiovascular Events: During the 12-month period, only one event each of myocardial infarction and stroke were observed. The study claims that the incidence did not differ significantly from the expected rate in this type of patient cohort, suggesting that the dual therapy neither increased nor decreased the cardiovascular risk substantially.

Interpretation: The dual therapy with Metformin and ACE Inhibitors significantly improved glycemic control and reduced blood pressure, which are both crucial in managing diabetes and reducing cardiovascular risk.

However, the therapy did not have a significant impact on the lipid profile, which is another critical factor in cardiovascular health.

The low incidence of cardiovascular events is encouraging but not sufficient to make any definitive conclusions about the therapy's effectiveness in reducing such events, primarily due to the limited sample size and follow-up duration.

This study suggests that while Metformin and ACE Inhibitors can be effective in managing glycemic levels and blood pressure in Type 2 Diabetes patients, they might not be sufficient for comprehensive cardiovascular risk management, as indicated by the unchanged lipid profile.

Table 1: Demographic Characteristics of Study Participants

Parameter	Data	Interpretation
Gender	55 Male, 45 Female	Balanced gender distribution
Mean Age (years)	55.4 ± 6.9	Middle-aged, typical for Type 2 Diabetes

Table 2: Changes in Glycemic Control (HbA1c Levels) Among Study Participants

Time Point	Mean HbA1c (%)	Statistical Significance	Interpretation
Baseline	8.2 ± 0.5	-	Initial level
6 Months	7.5 ± 0.4	$p < 0.05$ vs. Baseline	Improved
12 Months	7.1 ± 0.4	$p < 0.01$ vs. Baseline	Further Improved

Table 3: Longitudinal Changes in Blood Pressure (mmHg) Among Study Participants

Time Point	Mean Systolic	Mean Diastolic	Statistical Significance	Interpretation
Baseline	142.6 ± 8.3	89.2 ± 5.8	-	Initial level
6 Months	130.5 ± 7.9	83.6 ± 5.1	$p < 0.05$ vs. Baseline	Improved
12 Months	128.1 ± 7.1	80.9 ± 4.9	$p < 0.01$ vs. Baseline	Further Improved

Table 4: Longitudinal Assessment of Lipid Profile (mg/dL) Among Study Participants

Parameter	Baseline	12 Months	Statistical Significance
Total Cholesterol	200.1 ± 17.2	198.5 ± 16.5	$p > 0.05$
LDL Cholesterol	110.3 ± 10.6	109.8 ± 10.2	$p > 0.05$

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HDL Cholesterol	44.1 ± 4.7	44.5 ± 4.8	p > 0.05
Triglycerides	162.4 ± 13.8	161.6 ± 13.3	p > 0.05

Table 5: Incidence of Cardiovascular Events Among Study Participants

Parameter	Incidents
Myocardial Infarction	1 event
Stroke	1 event

DISCUSSION

Glycemic Control: Corroborating Prior Research

Our findings on glycemic control, as indicated by the reduction in mean HbA1c levels, concur with existing studies such as the one by Kenny HC et al. (2019).[1] This prior research also showed a significant drop in HbA1c levels for patients on dual therapy with Metformin and ACE Inhibitors (ADA, 20173,[4] Patel et al,[7] 2008 Duckworth et al., 2009),[8] thereby substantiating our results. The importance of effective glycemic management is further emphasized by the risk of long-term diabetes complications, a notion supported by multiple studies (Kenny HC & Abel ED, 20191; Guariguata et al., 2014).[2]

Blood Pressure: A Consistent Finding

The study's observations on the reduction in both systolic and diastolic blood pressure are in line with existing literature, including the study by Rubler S et al,[6] (1972). Previous research has consistently indicated that the dual therapy under consideration effectively lowers blood pressure, which is pivotal given the known cardiovascular risks associated with hypertension in diabetic patients (Gerstein et al., 2007; Gudmundsdottir et al., 2006).[13,14]

Lipid Profile: A Departure from Previous Studies

Contrary to previous findings by Jeon JY et al. (2021),[10] our study did not indicate significant changes in lipid profiles. This discrepancy, alongside the lack of statistical significance in our p-values, suggests that dual therapy may not be universally effective for lipid management in Type 2 Diabetes Mellitus patients (Foretz et al., 2014; Jeon et al., 2021).[9,10] This calls for more targeted research to understand the influencing factors such as lifestyle habits or other medications.

Cardiovascular Events: Need for Larger Studies

While the incidence of cardiovascular events in our study was low, the limited sample size and follow-up duration render these findings inconclusive. Gerstein HC et al,[13] (2016) have emphasized the necessity for larger sample sizes and longer study durations to confirm cardiovascular outcomes in diabetes treatment (International Diabetes Federation, 2016; Grundy et al., 1999).[12]

In summary, our study corroborates existing research regarding the benefits of Metformin and ACE Inhibitors on glycemic control and blood pressure in Type 2 Diabetes Mellitus patients (Kaĭdashev et al., 2010).[15] However, the results indicate that the therapy may not uniformly improve lipid profile or reduce cardiovascular risk, echoing the need for more comprehensive and long-term research to validate these findings (ADA, 2014; Kannel & McGee, 1979).[5]

CONCLUSION

In this 12-month longitudinal study, dual therapy with Metformin and ACE Inhibitors significantly improved glycemic control and blood pressure in Type 2 Diabetes Mellitus patients. However, no marked effect was observed on lipid profiles or cardiovascular events. These mixed results highlight the need for broader, long-term studies to fully assess the therapy's efficacy in comprehensive diabetes and cardiovascular risk management.

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