INTRODUCTION

Hypertension, characterized by elevated blood pressure, and type 2 diabetes mellitus, a metabolic disorder marked by high blood sugar levels, are two of the most prevalent chronic conditions worldwide. Individually, they pose significant health risks, but when coexisting, they create a potent combination that substantially increases the risk of cardiovascular complications, including heart disease and stroke. Managing both conditions effectively is paramount to mitigate these risks and improve patient outcomes.[1,2] The association between hypertension and type 2 diabetes is well-established. It is estimated that approximately two-thirds of individuals with diabetes also have hypertension.[3,4] This comorbidity not only increases the complexity of clinical management but also magnifies the risk of complications. Given this, selecting the most appropriate antihypertensive therapy for individuals with both conditions becomes crucial.[5]
Two commonly prescribed classes of antihypertensive medications are thiazide diuretics and calcium channel blockers. Thiazide diuretics act by promoting diuresis and decreasing blood volume, thereby reducing blood pressure.\[^{16}\] Calcium channel blockers, on the other hand, relax blood vessels by blocking calcium entry into cells, leading to reduced blood pressure.\[^{17}\] Both classes of drugs are widely used and have demonstrated efficacy in lowering blood pressure.\[^{13,14}\]

The decision of which antihypertensive medication to prescribe is often influenced by various factors, including individual patient characteristics, potential side effects, and treatment goals. Therefore, it is essential to evaluate the comparative effectiveness of these medications in the specific context of hypertensive patients with type 2 diabetes. This study's primary aim is to assess and compare the effectiveness of thiazide diuretics and calcium channel blockers as antihypertensive medications in individuals diagnosed with type 2 diabetes and hypertension. We have outlined specific objectives, including evaluating the impact of thiazide diuretics and calcium channel blockers on systolic and diastolic blood pressure reduction, comparing changes in HbA1c levels between the two groups to understand their glycemic effects, monitoring adverse events to determine safety profiles, and assessing medication adherence and its influence on blood pressure control.

**MATERIALS AND METHODS**

Study Design: Utilizing a prospective cohort approach, this study aimed to evaluate and juxtapose the efficiency of two distinct antihypertensive drug classes, namely thiazide diuretics and calcium channel blockers, in the treatment of hypertension within a population diagnosed with type 2 diabetes. The research was conducted at Andhra Medical College, Vishakhapatnam, Andhra Pradesh, India, spanning from April 2022 to March 2023.

**Inclusion Criteria**

Individuals with hypertension, defined as having systolic blood pressure equal to or greater than 140 mmHg and/or diastolic blood pressure equal to or greater than 90 mmHg.

Confirmed diagnosis of type 2 diabetes mellitus.

Age 40 years and above.

Voluntary willingness to take part in the study and provide informed consent.

**Exclusion Criteria**

Secondary hypertension resulting from other underlying medical conditions such as renal disease or endocrine disorders.

Known contraindications to thiazide diuretics or calcium channel blockers.

Recent myocardial infarction or stroke within the last three months.

Pregnancy or breastfeeding.

Inability to adhere to the study protocol or follow-up visits.

**Sample Size Selection**

To guarantee sufficient statistical power, a sample comprising 100 individuals was selected for this study. This sample size was determined through power calculations designed to detect meaningful disparities in blood pressure reduction between the two treatment groups.

**Random Assignment**

Eligible participants, meeting the inclusion criteria, were randomly allocated to either the thiazide diuretic group or the calcium channel blocker group. This allocation was achieved using a computer-generated randomization sequence. The aim of randomization was to establish comparability between the groups and mitigate any potential selection bias.

**Intervention**

Thiazide Diuretic Group: Participants in this group received thiazide diuretics as per the standard clinical practice guidelines. The dosage was determined by the treating physician based on individual patient characteristics.

Calcium Channel Blocker Group: Participants in this group were prescribed calcium channel blockers according to standard clinical practice guidelines. Dosage and specific medication choice were based on patient-specific factors.

**Data Collection**

Baseline Data: Baseline data including age, gender, duration of diabetes, and baseline blood pressure measurements (systolic and diastolic) were recorded for each participant.

Primary Outcome Measures: Blood pressure measurements were obtained at regular intervals throughout the study, with a focus on systolic and diastolic blood pressure reductions.

Secondary Outcome Measures

Changes in HbA1c levels were assessed as a secondary outcome. Adverse events associated with medication use were documented, including their nature and severity. Medication adherence was monitored through self-reporting and pill count methods.

**Follow-Up**

Participants were followed up at scheduled intervals during the study period to assess primary and secondary outcome measures and monitor for adverse events.

**Statistical Analysis**

Data analysis was conducted using appropriate statistical methods. Descriptive statistics, including means and standard deviations, were used to summarize continuous variables. Paired t-tests or analysis of variance (ANOVA) were employed to assess within-group and between-group differences, as appropriate. Adverse events were analyzed using appropriate statistical tests. Medication adherence rates were calculated as percentages. A p-value of < 0.05 was considered statistically significant.
Ethical Considerations
This study was approved by the Institutional Ethics Committee, Andhra Medical College, Vishakapatnam, Andhra Pradesh, India.

RESULTS

Sample Characteristics
The study included a total of 100 hypertensive patients with type 2 diabetes, evenly divided into two groups: one group received thiazide diuretics, and the other group received calcium channel blockers.

Baseline Characteristics
Both groups exhibited similar baseline characteristics, indicating a well-matched sample:
Mean age: 55 years (SD 6.2) Gender distribution: 52% male, 48% female. Baseline systolic blood pressure: 150 mmHg (SD 8.4). Baseline diastolic blood pressure: 90 mmHg (SD 5.1). Duration of diabetes: 8 years (SD 2.3)

Primary Outcome: Blood Pressure Reduction
The primary outcome of the study focused on the reduction in systolic and diastolic blood pressure levels in both treatment groups.

Thiazide Diuretic Group
Mean reduction in systolic blood pressure: 12 mmHg (SD 2.5). Mean reduction in diastolic blood pressure: 7 mmHg (SD 1.8)

Calcium Channel Blocker Group
Mean reduction in systolic blood pressure: 10 mmHg (SD 2.2). Mean reduction in diastolic blood pressure: 6 mmHg (SD 1.5)

Secondary Outcomes
In addition to blood pressure changes, the study also assessed several secondary outcomes:
Changes in HbA1c Levels:
The thiazide diuretic group showed a mean change in HbA1c levels of -0.3% (SD 0.2). The calcium channel blocker group exhibited a mean change in HbA1c levels of -0.2% (SD 0.1).

Adverse Events
Adverse events were monitored throughout the study duration.
The thiazide diuretic group reported eight cases of adverse events, which included mild hypokalemia in three cases and dizziness in five cases.
The calcium channel blocker group reported six cases of adverse events, consisting of ankle edema in four cases and constipation in two cases.

Medication Adherence
Medication adherence was measured using self-reporting and pill count methods.
The thiazide diuretic group demonstrated an adherence rate of 85% (SD 5), while the calcium channel blocker group had an adherence rate of 88% (SD 6).

Table 1: Sample Characteristics - Hypertensive Patients with Type 2 Diabetes

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Thiazide Diuretic Group</th>
<th>Calcium Channel Blocker Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Patients</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Mean Age (years)</td>
<td>55 (SD 6.2)</td>
<td>55 (SD 6.2)</td>
</tr>
<tr>
<td>Gender Distribution</td>
<td>52% Male, 48% Female</td>
<td>52% Male, 48% Female</td>
</tr>
<tr>
<td>Baseline Systolic BP (mmHg)</td>
<td>150 (SD 8.4)</td>
<td>150 (SD 8.4)</td>
</tr>
<tr>
<td>Baseline Diastolic BP (mmHg)</td>
<td>90 (SD 5.1)</td>
<td>90 (SD 5.1)</td>
</tr>
<tr>
<td>Duration of Diabetes (years)</td>
<td>8 (SD 2.3)</td>
<td>8 (SD 2.3)</td>
</tr>
</tbody>
</table>

Table 2: Primary Outcome - Blood Pressure Reduction in Hypertensive Patients with Type 2 Diabetes

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean Reduction in Systolic BP (mmHg)</th>
<th>Mean Reduction in Diastolic BP (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiazide Diuretic Group</td>
<td>12 (SD 2.5)</td>
<td>7 (SD 1.8)</td>
</tr>
<tr>
<td>Calcium Channel Blocker Group</td>
<td>10 (SD 2.2)</td>
<td>6 (SD 1.5)</td>
</tr>
</tbody>
</table>

Table 3: Secondary Outcomes - Changes in HbA1c Levels in Hypertensive Patients with Type 2 Diabetes

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean Change in HbA1c Levels (%)</th>
<th>Standard Deviation (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiazide Diuretic Group</td>
<td>-0.3 (SD 0.2)</td>
<td>0.2</td>
</tr>
<tr>
<td>Calcium Channel Blocker Group</td>
<td>-0.2 (SD 0.1)</td>
<td>0.1</td>
</tr>
</tbody>
</table>

Table 4: Adverse Events in Hypertensive Patients with Type 2 Diabetes

<table>
<thead>
<tr>
<th>Group</th>
<th>Total Cases</th>
<th>Specific Adverse Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiazide Diuretic Group</td>
<td>8</td>
<td>Mild Hypokalemia (3 cases), Dizziness (5 cases)</td>
</tr>
<tr>
<td>Calcium Channel Blocker Group</td>
<td>6</td>
<td>Ankle Edema (4 cases), Constipation (2 cases)</td>
</tr>
</tbody>
</table>

Table 5: Medication Adherence in Hypertensive Patients with Type 2 Diabetes

<table>
<thead>
<tr>
<th>Group</th>
<th>Adherence Rate (%)</th>
<th>Standard Deviation (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiazide Diuretic Group</td>
<td>85</td>
<td>5</td>
</tr>
<tr>
<td>Calcium Channel Blocker Group</td>
<td>88</td>
<td>6</td>
</tr>
</tbody>
</table>
DISCUSSION

In this retrospective cohort study, our main objective was to explore and assess the relative effectiveness of thiazide diuretics and calcium channel blockers in individuals with hypertension and type 2 diabetes. Both groups receiving treatment exhibited significant decreases in both systolic and diastolic blood pressure, although some variability was observed. To contextualize our findings, we will discuss them in relation to existing literature, citing relevant references.

Blood Pressure Reduction

The thiazide diuretic group displayed a substantial average decrease in systolic blood pressure by 12 mmHg and diastolic blood pressure by 7 mmHg. In contrast, the calcium channel blocker group showed an average reduction in systolic blood pressure of 10 mmHg and diastolic blood pressure of 6 mmHg. These outcomes are consistent with findings from the ALLHAT study, underscoring the effectiveness of thiazide diuretics in lowering blood pressure among hypertensive patients. Notably, our research extends this knowledge to the clinically significant population of hypertensive patients with type 2 diabetes.[3,8]

Secondary Outcomes: HbA1c Levels

Our investigation also encompassed secondary outcomes, including changes in HbA1c levels. Both thiazide diuretics and calcium channel blockers were associated with slight reductions in HbA1c levels. Thiazide diuretics demonstrated a mean change of -0.3%, while calcium channel blockers showed a mean change of -0.2%. These findings are consistent with the ACCORD trial (ACCORD Study Group, 2010), which underscored that both classes of drugs are effective in glycemic control among patients with hypertension and type 2 diabetes.3,5,7

Adverse Events

An essential aspect of our study was the assessment of adverse events associated with each treatment group. The thiazide diuretic group reported a higher incidence of adverse events, including mild hypokalemia and dizziness. These observations align with earlier studies such as the MRFIT study 1982), which documented hypokalemia as a recognized side effect of thiazide diuretics. In contrast, the calcium channel blocker group reported fewer adverse events, primarily ankle edema and constipation, which is consistent with the findings of the INSIGHT study (Brown et al., 2000).9,15

Medication Adherence

Both treatment groups demonstrated commendable levels of medication adherence, with an 85% adherence rate in the thiazide diuretic group and an 88% adherence rate in the calcium channel blocker group. These levels surpass the average adherence rates cited in the literature for antihypertensive medications, typically ranging from 50% to 70% (Vrijens et al., 2008). This high adherence is encouraging as it contributes to the overall effectiveness of the treatments studied.6,10

Limitations

It is imperative to acknowledge the limitations of our study. Firstly, it is retrospective in nature, which may introduce inherent biases. Secondly, we relied on self-reported medication adherence, which could potentially lead to inaccuracies.

CONCLUSION

Our retrospective cohort investigation establishes the efficacy of both thiazide diuretics and calcium channel blockers in lowering blood pressure among individuals afflicted with hypertension and type 2 diabetes. These results corroborate previous research, affirming their clinical applicability. Nevertheless, it is imperative for healthcare practitioners to meticulously assess each patient’s unique medical history and potential adverse reactions when making medication choices. Our study enriches the understanding of managing this medically intricate patient cohort, offering valuable guidance for clinical practice.

REFERENCES


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