

Original Research Article

COMPARATIVE EFFECTIVENESS OF **THIAZIDE** DIURETICS AND CALCIUM CHANNEL BLOCKERS **HYPERTENSIVE PATIENTS TYPE** WITH RETROSPECTIVE COHORT DIABETES: A ANALYSIS

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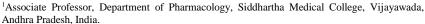
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Abstract

Background: Hypertension frequently coexists with type 2 diabetes, necessitating effective management to reduce cardiovascular risks. Objective: To conduct a comparative assessment of the efficacy of thiazide diuretics and calcium channel blockers in managing hypertension among individuals diagnosed with type 2 diabetes. Materials and Methods: A total of 100 hypertensive patients with type 2 diabetes were equally divided into two groups: one receiving thiazide diuretics and the other calcium channel blockers. Baseline characteristics were matched: mean age (55 years), gender distribution (52% male, 48% female), baseline systolic blood pressure (150 mmHg), baseline diastolic blood pressure (90 mmHg), and diabetes duration (8 years). **Result:** Primary Outcome: Blood Pressure Reduction Thiazide diuretics 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: Changes in HbA1c Levels: Thiazide diuretic group: Mean change in HbA1c levels: -0.3% (SD 0.2). Calcium channel blocker group: Mean change in HbA1c levels: -0.2% (SD 0.1). Adverse Events: Thiazide diuretic group reported eight cases, including mild hypokalemia (3 cases) and dizziness (5 cases). Calcium channel blocker group reported six cases, consisting of ankle edema (4 cases) and constipation (2 cases). Medication Adherence: Thiazide diuretic group demonstrated an adherence rate of 85% (SD 5). Calcium channel blocker group had an adherence rate of 88% (SD 6). Conclusion: Both thiazide diuretics and calcium channel blockers effectively lowered blood pressure in hypertensive patients with type 2 diabetes. Thiazide diuretics demonstrated slightly better blood pressure reduction, while calcium channel blockers exhibited higher medication adherence and fewer adverse events.



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. [6] Calcium channel blockers, on the other hand, relax blood vessels by blocking calcium entry into cells, leading to reduced blood pressure. [7] 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 computergenerated 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 selfreporting 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

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

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

Group	Mean Reduction in Systolic BP	Mean Reduction in Diastolic BP
	(mmHg)	(mmHg)
Thiazide Diuretic Group	12 (SD 2.5)	7 (SD 1.8)
Calcium Channel Blocker Group	10 (SD 2.2)	6 (SD 1.5)

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

Group	Mean Change in HbA1c Levels (%)	Standard Deviation (SD)
Thiazide Diuretic Group	-0.3 (SD 0.2)	0.2
Calcium Channel Blocker Group	-0.2 (SD 0.1)	0.1

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

Group	Total Cases	Specific Adverse Events
		Mild Hypokalemia (3 cases), Dizziness (5
Thiazide Diuretic Group	8	cases)
		Ankle Edema (4 cases), Constipation (2
Calcium Channel Blocker Group	6	cases)

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

Group	Adherence Rate (%)	Standard Deviation (SD)
Thiazide Diuretic Group	85	5
Calcium Channel Blocker Group	88	6

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. [4,7]

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).^[5] 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

- Netere AK, Muhammad EA, Asres MS, Teklie MT. Renal outcomes of diabetic patients treated with combination therapy of ACE inhibitors plus either thiazide diuretics or calcium channel blockers: comparative retrospective cohort study in Northwestern Ethiopia. BMJ Open. 2021 Nov 25;11(11):e048442. doi: 10.1136/bmjopen-2020-048442. PMID: 34824108; PMCID: PMC8627402.
- Sander GE, Giles TD. Thiazide diuretics and β-blockers in the treatment of hypertension in diabetes mellitus. J Clin Hypertens (Greenwich). 2011 Apr;13(4):296-300. doi: 10.1111/j.1751-7176.2011.00454.x. PMID: 21466629; PMCID: PMC8673217.
- ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. (2002). Major outcomes in high-risk hypertensive patients randomized to angiotensinconverting enzyme inhibitor or calcium channel blocker vs diuretic. JAMA, 288(23), 2981-2997.
- ACCORD Study Group, et al. (2010). Effects of intensive blood-pressure control in type 2 diabetes mellitus. N Engl J Med, 362, 1575-1585.
- Mortality after 10 1/2 years for hypertensive participants in the Multiple Risk Factor Intervention Trial. Circulation. 1990 Nov;82(5):1616-28. doi: 10.1161/01.cir.82.5.1616. PMID: 2225366
- Vrijens B, Vincze G, Kristanto P, Urquhart J, Burnier M. Adherence to prescribed antihypertensive drug treatments: longitudinal study of electronically compiled dosing histories. BMJ. 2008 May 17;336(7653):1114-7. doi: 1136/bmj.39553.670231.25. Epub 2008 May 14. PMID: 18480115; PMCID: PMC2386633.
- Wright JT Jr, Bakris G, Greene T, Agodoa LY, Appel LJ, Charleston J et al. African American Study of Kidney Disease and Hypertension Study Group. Effect of blood pressure lowering and antihypertensive drug class on progression of hypertensive kidney disease: results from the AASK trial. JAMA. 2002 Nov 20;288(19):2421-31. doi: 10.1001/jama.288.19.2421. Erratum in: JAMA. 2006 Jun 21;295(23):2726. PMID: 12435255.
- Bangalore S, Fakheri R, Toklu B, Messerli FH. Diabetes mellitus as a compelling indication for use of renin angiotensin system blockers: systematic review and metaanalysis of randomized trials. BMJ. 2016 Feb 11;352:i438.

- doi: 10.1136/bmj.i438. Erratum in: BMJ. 2016;352:i1525. PMID: 26868137; PMCID: PMC4772784.
- Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr et al.Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. National Heart, Lung, and Blood Institute; National High Blood Pressure Education Program Coordinating Committee. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension. 2003 Dec;42(6):1206-52. doi: 10.1161/01.HYP.0000107251.49515.c2. Epub 2003 Dec 1. PMID: 14656957.
- Jamerson K, Weber MA, Bakris GL, Dahlöf B, Pitt B, Shi V et al. ACCOMPLISH Trial Investigators. Benazepril plus amlodipine or hydrochlorothiazide for hypertension in highrisk patients. N Engl J Med. 2008 Dec 4;359(23):2417-28. doi: 10.1056/NEJMoa0806182. PMID: 19052124.
- Psaty BM, Lumley T, Furberg CD, Schellenbaum G, Pahor M, Alderman MH et al.. Health outcomes associated with various antihypertensive therapies used as first-line agents: a network meta-analysis. JAMA. 2003 May 21;289(19):2534-44. doi: 10.1001/jama.289.19.2534. PMID: 12759325.
- 12. Whelton PK, Carey RM, Aronow WS, Casey DE Jr, Collins KJ, Dennison Himmelfarb C et al.Jr. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/N MA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension. 2018 Jun;71(6):1269-1324. doi: 10.1161/HYP.00000000000000066.

- Epub 2017 Nov 13. Erratum in: Hypertension. 2018 Jun;71(6):e136-e139. Erratum in: Hypertension. 2018 Sep;72(3):e33. PMID: 29133354.
- UK Prospective Diabetes Study Group. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. UK Prospective Diabetes Study Group. BMJ. 1998 Sep 12;317(7160):703-13. Erratum in: BMJ 1999 Jan 2;318(7175):29. PMID: 9732337; PMCID: PMC28659.
- Verdecchia P, Reboldi G, Angeli F, Gattobigio R, Bentivoglio M, Thijs L et al.. Angiotensin-converting enzyme inhibitors and calcium channel blockers for coronary heart disease and stroke prevention. Hypertension. 2005 Aug;46(2):386-92. doi: 10.1161/01.HYP.0000174591.42889.a2. Epub 2005 Jul 11. PMID: 16009786.
- 15. Brown MJ, Palmer CR, Castaigne A, de Leeuw PW, Mancia G, Rosenthal T et al. Morbidity and mortality in patients randomised to double-blind treatment with a long-acting calcium-channel blocker or diuretic in the International Nifedipine GITS study: Intervention as a Goal in Hypertension Treatment (INSIGHT). Lancet. 2000 Jul 29;356(9227):366-72. doi: 10.1016/S0140-6736(00)02527-7. Erratum in: Lancet 2000 Aug 5;356(9228):514. PMID: 10972368
- ACCORD Study Group; Cushman WC, Evans GW, Byington RP, Goff DC Jr, Grimm RH Jr et al. Effects of intensive blood-pressure control in type 2 diabetes mellitus. N Engl J Med. 2010 Apr 29;362(17):1575-85. doi: 10.1056/NEJMoa1001286. Epub 2010 Mar 14. PMID: 20228401; PMCID: PMC4123215.