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Research Article

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Study of Prescribing Pattern and Evaluation of the Efficacy of Monotherapy vs. Polytherapy Antihypertensive Drugs in Diabetes Patients

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Abstract: The monitoring pattern of antihypertensive drugs and evaluation of the efficacy of prescribed pharmacological regimen can provide important vision into control of hypertension and prevention of related comorbidities. This study aimed to evaluate prescribing patterns and efficacy of prescribed monotherapy vs. polytherapy antihypertensive drugs in diabetes patients. A hospital-based prospective study was conducted in the medicine department of Kempegowda Institute of Medical Sciences Hospital and Research Center, Bangalore, India for a duration of 12 months. A total of 720 hypertensive patients with type 2 diabetes mellitus aged = 18 years were included in this study. Ninety patients (31%) were presented with chronic kidney disease, followed by ischemic heart disease (82, 28.3%), stroke (78, 26.9%), and heart failure (40, 13.8%). Monotherapy was prescribed more commonly than polytherapy (60.14% vs. 39.86%). The majority of patients were treated with Calcium channel blockers. In both therapeutic regimens, mono- and polytherapy, amlodipine was found to be the most prescribed drug. Comparison between results of antihypertensive monotherapy and polytherapy regimens (a combination of different classes of antihypertensive drugs) revealed that only prescription of polytherapy was associated with a statistically significant reduction in both systolic and diastolic blood pressure (mean (SD) of systolic blood pressure before polytherapy vs. after polytherapy; 166 (3.2) vs. 139 (1.4), < 0.0001. mean (SD) of diastolic blood pressure before polytherapy vs. after polytherapy; 103 (1.6) vs. 88 (0.5), < 0.0001). Systolic/diastolic blood pressure was not controlled and maintained within a therapeutic goal among patients who received single antihypertensive medication (monotherapy). Therefore, a combination of antihypertensive medications needs to be considered to achieve controlled blood pressure and avoid clinical inertia among hypertensive patients with diabetes.

Keywords: Hypertension, Type 2 Diabetes Mellitus, Prescribing Pattern, Antihypertensive Drugs, Polytherapy, Clinical Inertia

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1. INTRODUCTION

Hypertension is considered to be a common medical illness, which is defined as "persistently elevated arterial blood pressure" (BP).[1] High BP is a well-established risk factor for the occurrence of different types of cardiovascular diseases (CVD) like acute coronary artery disease, myocardial infarction, and cerebrovascular accident. Moreover, high BP is the fourth and seventh leading cause of mortality in developed countries and under developing countries, respectively. Nearly 40% of adult people in the South-east Asian region are reported to have hypertension. Several studies have been conducted in the municipal and countryside of India, which indicate the great interest of researchers about this very common risk factor of CVD.[2, 3] The pharmacotherapeutic guidelines for the management of hypertension and Cardiology Societies recommend the overall therapeutic goal of high BP is the reduction of morbidity, mortality, and complications associated with hypertension.[4, 5] High BP has a great mortality rate with an annually steady increasing rate of occurrence among the adult population. For example, one out of three adults (around 1 billion people) globally are affected by systemic hypertension, and the estimated number will increase to 1.6 billion by 2025.[6] Hypertension is the main reason for the increased risk of morbidity and mortality among patients with diabetes. In other words, a combination of systemic hypertension and diabetes further increases the risk of associated complications like nephropathy, chronic kidney failure, retinopathy, and neuropathy.[7] In addition, CVD is the main cause of mortality and morbidity in patients with type 2 diabetes. There are several risk factors, including tobacco smoking, high BP, and dyslipidemia, that have been shown to speed up the development of CVD.[8] Worldwide prevalence of diabetes among adults (aged 20–79 years) revealed that from 2010 to 2030, there will be up to 50% increase in the number of patients diagnosed with diabetes of which up to 40% increase is predicted to occur in India and China, respectively.[9] Although lifestyle modification shows a positive impact in the management of systemic hypertension, the majority of hypertensive patients need a combination of at least two antihypertensive medications to control their BP and maintain it within a therapeutic goal.[7, 10, 11] Randomized clinical trials demonstrated that medication therapy of hypertensive diabetes patients with purpose reduction and maintaining BP within therapy goal was associated with a reduction of diabetes-related macro- and microvascular complications.[12] The 2014 Evidence-Based Guideline for the Management of High Blood Pressure in adults, the Eighth Joint National Committee (JNC 8) recommends for a combination of four different classes of antihypertensive medications which include thiazide diuretic, calcium channel blocker, an angiotensin-converting enzyme inhibitor, and angiotensin receptor blocker for management of hypertensive patients diagnosed with diabetes. The purpose of this combination a therapy is to maintain therapy goal of lower than 140 mmHg for systolic BP and 90 mmHg for diastolic BP among hypertensive patients aged 18 years or older with diabetes.[13] Therefore, our study aimed to evaluate the prescribing pattern and the efficacy of prescribed antihypertensive drugs (monotherapy vs. polytherapy) in maintaining BP goals in hypertensive patients with diabetes.

2. MATERIALS AND METHODS

2.1. Study design and setting

A hospital-based prospective study was conducted for one year in the Medicine Department of Kempegowda Institute of Medical Sciences Hospital (KIMS) and Research Center, Bangalore, India.

2.2. Inclusion Criteria

Patients (aged 18 years and above, any gender) who were diagnosed with hypertension (according to the definition of JNC-8 guideline[13]) and type 2 diabetes admitted to the Medicine Department of the KIMS Hospital and Research Center, Bangalore, India.

2.3. Exclusion Criteria

Type 1 diabetic patients, gestational hypertension, and breast-feeding women were excluded.

2.4. Study process

The study received ethical approval from the Institutional Human Ethics Committee of the Department of Pharmacy Practice. (Reference number: VIPS/IEC/2018/08). Through the study process, all patient- and medication-related data were documented in a suitably designed data collection form. All data relevant to the study was obtained from patient case sheets, medication charts, and laboratory reports. Data was collected with respect to demographic details (name, age, and sex of patients), diagnosis, admission and discharge date. The prescribed drug data including brand and generic name of all antihypertensive drugs, dose, dose frequency and route of administration were recorded. Patients` medication charts were reviewed to identify the current prescribing pattern of antihypertensive drugs. Patients` BP before and after receiving antihypertensive regimens (mono- and polytherapy) were recorded for further statistical analysis. Results of single antihypertensive therapy (monotherapy) and combination therapy (polytherapy) were compared to evaluate the efficacy of antihypertensive drugs regimen in maintaining BP goals among patients.

3. STATISTICAL ANALYSIS

Descriptive statistics were applied for calculation of mean, standard deviation, frequencies, and percentages of patient's demographic/clinical characteristics, and medication-related data. Student's t-test was applied for comparison between mean (SD) results obtained from single antihypertensive therapy (monotherapy) and combination therapy (polytherapy). A P value of < 0.05 was defined as statistically significant. The Statistical Package for Social Sciences for Windows, version 22.0 was used for data analysis. [14]

4. RESULTS

A total of 720 hypertensive patients with type 2 diabetes mellitus were included during the period of study, of which 61%, 39% were male and female, respectively. The mean (SD) of patient's age was 58.1±12.8 years. Among hypertensive patients with diabetes, 290 (40.3%) patients were presented with the comorbidities, which included chronic kidney disease (90, 31%), ischemic heart disease (82, 28.3%), stroke (78, 26.9%), and heart failure (40, 13.8%) (Table 1).

Table 1. Demographic and clinical characteristics of patients	
Total number of patients	**N = 720, n (%)**
Age in years (mean ± standard deviation)	58.1 ± 12.8
Male	438 (61%)
Female	282 (39%)
Number of morbidities	**N = 290, n (%)**
Chronic kidney disease	90 (31)
Ischemic heart disease	82 (28.3)
Stroke	78 (26.9)
Heart failure	40 (13.8)

In our observation, the highest number of patients with stroke were females aged 55-74 years, which showed more than twice the proportion of stroke occurrence in comparison with men at same age distribution; female: 51.28% vs. male: 24.36% (Table 2).

Table 2. Incidence of stroke in relation to age distribution and gender of study patients				
Age distribution	**Stroke among male patients**		**Stroke among female patients**	
	N	**(%)**	**N**	**(%)**
30-54	3	3.85	2	2.56
55-74	19	24.36	40	51.28
≥ 75	2	2.56	12	15.38

Through the process of medication chart review, we identified that patients were treated with different classes of antihypertensive drugs, of which 60.14% of patients received monotherapy and 39.86% received polytherapy for controlling their high BP. Calcium channel blocker (418, 34.09%), loop diuretic (243, 19.82%), angiotensin receptor blocker (186, 15.17%), and β blocker (161, 13.13%) were the most common prescribed antihypertensive classes of medications. The total number of drugs prescribed was 1226, and amlodipine (356, 29.04%) was found to be the most commonly prescribed drug, followed by furosemide (214, 17.46%) and telmisartan (152, 12.4%) (Table 3).

Table 3. Prescribing pattern of antihypertensive classes of medications		
Prescription pattern	**N**	**%**
Monotherapy	433	60.14
polytherapy	287	39.86
Polytherapy		
Two Drugs Combination	129	17.92
Three Drugs Combination	106	14.72
Four and more Drugs Combination	52	7.22
Antihypertensive drug classes		
Calcium Channel Blocker	418	34.09
Loop Diuretic	243	19.82
Angiotensin Receptor Blocker	186	15.17
β Blocker	161	13.13
α Blocker	79	6.44
Angiotensin Converting Enzyme Inhibitor	50	4.08
Thiazide Diuretic	36	2.94
Centrally Acting Agent	33	2.69
Vasodilator	20	1.63
Most prescribed antihypertensive drugs		
Amlodipine	356	29.04
Furosemide	214	17.46
Telmisartan	152	12.40
Metoprolol	86	7.01
Prazosin	79	6.44
Cilnidipine	43	3.51
Hydrochlorothiazide	36	2.94
Carvedilol	36	2.94
Clonidine	33	2.69
Losartan	22	1.79

Mean (SD) of systolic and diastolic BP was calculated for patients who received single antihypertensive therapy (monotherapy) and combination therapy (polytherapy). Comparison between monotherapy and polytherapy showed that only a combination of antihypertensive medication (polytherapy) significantly reduced systolic and diastolic BP and maintained BP goals among hypertensive patients with diabetes (Table 4 & 5).

Table 4. Comparison between the mean of systolic and diastolic blood pressure before and after monotherapy			
Blood pressure	**Patients before monotherapy (N = 433)**	**Patients after monotherapy (N = 433)**	***p* Value**
Mean (SD) of systolic blood pressure	161 (1.9)	155 (1.8)	0.13075
Mean (SD) of diastolic blood pressure	102 (1.3)	100 (0.8)	0

SD, standard deviation.

Table 5. Comparison between the mean of systolic and diastolic blood pressure before and after polytherapy			
Blood pressure	**Patients before polytherapy (N = 287)**	**Patients after polytherapy (N = 287)**	***p* Value**
Mean (SD) of systolic blood pressure	166 (3.2)	139^ (1.4)	< 0.0001*
Mean (SD) of Diastolic blood pressure	103 (1.6)	88^ (0.5)	< 0.0001*

*SD, standard deviation. ^ Blood pressure at JNC 8 goal. *Statistically significant at p < 0.05.*

5. DISCUSSION

A hospital-based prospective study was conducted to identify the prescribing pattern of antihypertensive drugs among diabetes patients. Moreover, to evaluate the efficacy of antihypertensive drugs in maintaining BP goals among patients, we compared the mean (SD) BP results of single antihypertensive therapy (monotherapy) and combination therapy (polytherapy). Out of 720 patients, 61% male, and 39% of patients were females. The majority of patients were in the age group of 41-60 years, and women above 41 years were found to be more prone to hypertension than their younger counterparts. This finding can be related to postmenopausal hypertension in females and indicates potential physiological protection of estrogen-the female hormone. Blood pressure is typically lower in premenopausal women than in men. [15] Hypertension is considered to be a major risk factor for the high prevalence of cardiovascular diseases among women. Also, hypertension is a known leading cause of death among female patients.[16] Studies showed that postmenopausal hypertension in women is likely associated with several mechanisms and contributing factors. Mechanisms responsible for elevated BP in aging women can be due to activation of the renin-angiotensin system, obesity, sympathetic activation, physiological protective effect of estrogen, anxiety, and depression.[15] In addition, a review study of mechanism and therapy of postmenopausal hypertension revealed that the lack of regular physical exercise and high intake of dietary salt are important factors associated with both occurrence and worsening of postmenopausal hypertension.[17] Therefore, nonpharmacological interventions like salt restriction, weight reduction, increased consumption of fresh fruit, vegetables, and increased physical activity are recommended for controlling hypertension in patients with diabetes. [18] During the process of evaluation of the prescribing pattern, we detected that patients were treated with either a single antihypertensive drug (monotherapy) or a combination of different classes of antihypertensive drugs (polytherapy). The majority of patients received at least one out of four recommended antihypertensive classes of drugs, and few patients were prescribed other classes of antihypertensive drugs. Overall, calcium channel blockers remained the most commonly used antihypertensive drug class as monotherapy and polytherapy regimen. A study conducted by Michael A Weber, et al. with the aim to determine which combination therapy in patients with hypertension and diabetes most effectively decreases cardiovascular events. The authors concluded that the combination of renin-angiotensin system blockers with amlodipine compared with hydrochlorothiazide was superior in reducing cardiovascular diseases in patients with diabetes. [19] A review study was conducted with attempts to highlight the potential of calcium-channel blockers in the prevention of medical complications in hypertensive patients with diabetes mellitus. This review study also demonstrated the beneficial role of calcium channel blockers in the prevention of cardiovascular complications in hypertensive patients with diabetes. [20] Comparison between results of mono- and polytherapy revealed that a combination of different classes of antihypertensive medications was more effective to significantly reduce systolic/diastolic BP and maintain BP within a therapeutic goal (JNC 8 recommendations). The ultimate goal of any blood pressure-lowering therapy is to reverse the risk associated with elevated blood pressure and to prevent the cardiovascular complications associated with hypertension. Appropriate control of BP in patients with type 2 diabetes mellitus is associated with improved patients` clinical outcomes, a lower risk of mortality, and medical complications including cardiovascular events among these patients. [21, 22] Tight blood pressure control with a combination of different classes of antihypertensive drugs in patients with hypertension and type 2 diabetes achieve a clinically significant reduction in the risk of deaths related to diabetes, complications associated with diabetes, a progression of diabetic retinopathy, and deterioration in visual acuity.[23] The importance of treating hypertension aggressively to ensure attainment of controlled BP goals is well-established, and treatment to target levels will often require combination therapy with two or more antihypertensive agents. [7, 10-11] Likewise, our analysis showed that most of the hypertensive patients with diabetes mellitus required more than one class of antihypertensive medication for their BP goal achievement. Our analysis revealed that the prescription of a monotherapy regimen for controlling BP among hypertensive patients with diabetes led to clinical inertia; [24] although patients` high BP were reduced, their BP was uncontrolled and inconsistent with therapeutic goals available in standard guideline (JNC 8). [13]

6. CONCLUSION

The study data analysis showed that prescribing patterns of antihypertensive drugs in diabetes patients with hypertension comprised mono- and polytherapy regimens. The majority of

patients received a monotherapy antihypertensive regimen, which was found to be inadequate pharmacological therapy for the management of high BP. Comparison between results of mono- and polytherapy regimens showed that prescription of combination antihypertensive therapy (polytherapy) was associated significantly with reduction of systolic/diastolic BP, consequently maintaining BP within the therapeutic goal. We recommend more efforts for closing the gap between treatment and control to maximize therapeutic effects and avoid clinical inertia in hypertensive patients with type 2 diabetes mellitus.

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7. AUTHORS CONTRIBUTION STATEMENT

All authors had contributions to the study conception and design, data analysis and interpretation. Aghili performed a major contributor to the acquisition of patient-related data and writing the original manuscript.

8. CONFLICT OF INTEREST

Conflict of interest declared none.

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