RESEARCH ARTICLE

STUDY OF UTILIZATION PATTERN OF ANTI-HYPERTENSIVE DRUGS IN HYPERTENSIVE DIABETIC PATIENTS WITH OR WITHOUT REDUCED RENAL FUNCTION AT TERTIARY CARE TEACHING HOSPITAL

Jay Shah[1], Tejas Khakhkhar[1], Saurabh Bhirud[2], Rima B Shah[3], Sanjay Date[1]

[1] Department of Pharmacology, SBKS Medical College and Research Centre, Piparia, Vadodara, Gujarat, India

[2] Department of Medicine, SBKS Medical College and Research Centre, Piparia, Vadodara, Gujarat, India

[3] Department of Pharmacology, GMERS Medical College, Gandhinagar, Gujarat, India

Correspondence to: Rima B Shah (rima_1223@yahoo.co.in)

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ABSTRACT

Background: The benefits of optimum blood pressure (BP) control in patients with diabetes exceed the benefits of glycaemic control and extend to the prevention of both macro-vascular and micro-vascular complications in patients suffering from both hypertension and diabetes mellitus.

Aims & Objective: To investigate the utilization patterns of anti-hypertensive drugs and to evaluate blood pressure (BP) control among diabetic-hypertensive patients with and without reduced renal function.

Material and Methods: A prospective, observational study carried out at medicine department of SBKS Medical College and Research Centre, Piparia. The pattern of use of antihypertensive drugs in 50 hypertensive-diabetic patients was evaluated in correlation with its renal function and BP control achieved was compared in patients with and without reduced renal function.

Results: Total 63 antihypertensive medication episodes were prescribed for 50 patients. Out of which 76% patients were receiving 1 drug, 22% receiving 2 drugs and 2% receiving 3 drugs of different antihypertensive class. Most patients were receiving Angiotensin-Converting-Enzyme-Inhibitors (ACE-I)/Angiotensin-Receptor-Blockers (ARBs) (60%), followed by CCBs (24%), beta-blockers (20%), and diuretics (16%). Patients on monotherapy were mostly receiving ACE-I/ARB (65.78%). Beta blockers were more commonly prescribed in patients with reduced renal function ($p=0.005$). BP control was achieved in 63.15% patients in monotherapy and 33.33% in polytherapy group. Control of systolic and diastolic BP was significantly higher in patients without reduced renal function than patients with reduced renal function ($p<0.05$).

Conclusion: There was suboptimum use of combination therapy among diabetic-hypertensive patients in general and specifically in developing countries as reflected by control achieved in systolic and diastolic BP which requires concern of all healthcare professionals.

KEY-WORDS: Blood Pressure Control; Hypertensive – Diabetic Patients; Prescribing Patterns; Antihypertensive Drugs; Renal Function; Evidence Based Medicine

Introduction

Hypertension affects about 20-60% of patients with type-2 diabetes.[1] Serious cardiovascular events are more than twice likely in patients with diabetes and hypertension than either disease alone.[2] The benefits of tight blood pressure (BP) control in patients with diabetes exceed the benefits of tight glycaemic control and extend to the prevention of both macro-vascular and micro-vascular complications.[3] However, studies consistently demonstrate that most diabetic patients do not achieve recommended levels of BP control, and the majority have a BP of >140/90mmHg.[4–6]

There are a growing number of pharmacological treatment options for patients with hypertension. However, the choice of anti-hypertensive drug class is influenced by many factors such as age, stage of hypertension and the presence of co-morbid conditions. The seventh report of the Joint National Committee on the Prevention, Detection, Evaluation and Treatment of High Blood Pressure

(JNC) stated that angiotensin converting enzyme inhibitors (ACE-I) is an important component of most regimens to control BP in diabetic patients.[7] In these patients, ACE-I may be used alone, but are much more effective when combined with thiazide type diuretic or other anti-hypertensive drugs. The JNC seventh report recommended that the BP in diabetics should be controlled to levels of 130/80 mmHg or lower. Rigorous control of BP is paramount for reducing the progression of diabetic nephropathy to end-stage renal disease (ESRD). In hypertensive patients with chronic kidney disease (CKD), defined as a glomerular filtration rate (GFR) < 60 mL/min, the JNC seventh report recommended a goal BP of ≤ 130/80 mmHg and a need for using more than one anti-hypertensive drug to achieve this goal.[7] Actual drug utilization data in this special group of patients from the local population are very few.

Therefore the primary objectives of this study were: 1) to evaluate the utilization of anti-hypertensive drugs in hypertensive and diabetic patients, 2) to compare utilization of anti-hypertensive drugs for diabetic patients with reference to renal impairment status and 3) to assess BP control in this population.

Materials and Methods

Settings and Study Design

It was a prospective, observational study carried out at SBKS Medical Institute and Research centre, Piparia, Vadodara. The study protocol was approved by Institutional Ethics Committee (IEC). A total of 50 patients meeting inclusion criteria were enrolled in the study to evaluate the pattern of use of antihypertensive drugs in patients suffering from both diabetes mellitus and hypertension and its correlation with reduced renal function. All the patients were explained clearly about the nature and purpose of the study in the language they understand and consent was obtained before enrolling them for the study. Records of inpatients and outpatients from medicine department were collected.

Inclusion Criteria & Exclusion Criteria

Diabetic hypertensive patients of either sex and any age attending medicine OPD and/or admitted in medicine ward and patients willing to participate in the study were enrolled in the study while patients with any cardiovascular complication, like ischaemic heart disease (IHD), chronic heart failure (CHF) or renal complication like end stage renal disease (ESRD) etc. and seriously ill patients requiring ICU admission or stay were excluded from study.

Sample Size

The primary objective of the study was to evaluate the pattern of antihypertensive drug use among diabetic hypertensive patients. Assuming a prevalence rate of hypertension in diabetic patient as 70%[1] and taking allowable error as 20% of positive character, 42 patients were needed to give an estimate at a width of 5% and with 95% confidence interval. Therefore 50 patients were enrolled for the present study.[8]

Participants & Data Collection

All the patients were examined on the day of enrolment in study and relevant details like past and present history of disease, blood pressure, serum creatinine and random blood sugar (RBS), drug therapy used etc were noted in the structured case record form by the researcher. The primary researcher was the doctor but not involved in any therapeutic decision for the patients. Patients were visited once only on the day of enrolment. Patients were interviewed for about 10-20 minutes and past as well as present hospital records were referred for gathering necessary information. All the data was analysed subsequently for different drugs used for hypertension with respect to presence of renal function impairment as measured by creatinine clearance.

Outcome Measure

The achievement of target blood pressure (≤130/80mmhg) was taken as a primary outcome measure. Different antihypertensive drugs used & their correlation with renal function and impact on target blood pressure achievement was also evaluated. For the present study, Elevated or non-target BP was defined as greater than or equal to 130/80 mmHg, according to the JNC seventh report.[7,9] Reduced renal function or renal

impairment was defined as creatinine clearance (Cr Cl) ≤ 60 mL/min or glomerular filtration rate GFR < 60 mL/ min. Creatinine clearance and GFR were calculated from the serum creatinine levels using a Cockcroft-Gault equation.[9]

Statistical Analysis

Data were presented as actual frequencies, percentage, mean and standard deviation. Analysis was carried out using Microsoft excel 2010 version and chi-square test, "p" values equal to or less than 0.05 was considered as significant.

Results

A total of 50 participants were enrolled in the study meeting inclusion criteria, out of which 26 (52%) were males and 24 (48%) were females. The mean age (SD) of the patients was 56.04 ± 10.46 years. The most recently recorded values of systolic, diastolic BP and random blood glucose level were 151.17 ± 29.40; 86.22 ± 13.06 and 173.4 ± 65.38 mg/dl respectively. The mean serum creatinine of the patients was 1.21 ± 0.66 mL/min with Glomerular filtration rate (GFR) 76.9 ± 29.16 mL/min. Out of total 50, 19 patients (38%) had reduced renal function GFR < 60 mL/min. The recommended target BP of equal or lower than 130/80 mmHg was achieved in 28(56%) patients with drug therapy. Duration of hypertension was <1 year in 44% of cases, 1-2 years in 18% of cases, >3 years in 38% of cases with the mean of 1.88 ± 1.52 years which does not positively correlates with status of kidney function (p=0.11). Clinical and demographic characteristics of the study population are shown in table 1.

A total of 63 antihypertensive medication episodes were prescribed for 50 patients. Out of 50 patients, 38 (76%) were receiving 1 drug, 11 (22%) were receiving 2 drugs and 1 (2%) was receiving 3 drugs of different antihypertensive class. Most patients were receiving angiotensin converting enzyme inhibitors (ACE-I) or angiotensin receptor blockers (ARBs) 30 antihypertensive episode (60%), followed by calcium channel blockers (CCBs) (12, 24%), beta blockers (10, 20%), and diuretics (8, 16%). Patients on monotherapy were mostly receiving ACE-I/ARB (25, 65.78%) followed by beta blockers (5, 13.15%), CCBs (4, 0.52%), thiazide diuretics (2, 5.26%) and combined alpha and beta blocker 2 patients (5.26%). [Table 2]

Table-1: Demographic Data and Clinical Characteristic of Study Population (n=50)

Parameter		Patients (%)	Mean ± SD
Age		-	56.04 ± 10.46
Gender Ratio (M/F)		26/24 (52/48)	1.08 ratio
Average Duration of HT		50 (100)	1.88 ± 1.52
Heart Rate (beats/min)	60-100	50 (100)	82.64 ± 5.91
	>100	0	
SBP (mmHg)	≤130	30 (60)	151.17 ± 29.40
	>130	20 (30)	
DBP (mmHg)	≤80	30 (60)	86.22 ± 13.06
	>80	20 (30)	
GFR (ml/min)	≥90	31 (62)	76.9 ± 29.16
	<90	19 (38)	
RBS (mg/dl)	<200	40 (80)	173.4 ± 65.38
	≥200	10 (20)	

SD: Standard Deviation; HT: Hypertension; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; GFR: Glomerular Filtration Rate; RBS: Random Blood Sugar

Table-2: Patterns of Use of Anti-Hypertensive Drugs among Patients (Single - versus Multidrug Therapy)

Drug Class	Overall Prescription of Drug n=63 (%)	No. of Drugs Prescribed		
		One Drug n=38 (%)	Two Drugs n=22 (%)	Three Drugs n=3 (%)
ACEIs	16 (25.39)	16 (42.10)	0	0
ARB	14 (22.22)	9 (23.68)	4 (18.18)	1 (33.33)
CCB	12 (19.04)	4 (10.52)	8 (36.36)	0
β- Blocker	10 (15.87)	5 (13.15)	5 (22.72)	0
Thiazide	8 (12.69)	2 (5.26)	5 (22.72)	1 (33.33)
Combined α & β Blockers	3 (4.76)	2 (5.26)	0	1 (33.33)

ACEIs: Angiotensin Converting Enzyme Inhibitors; ARB: Angiotensin Receptor Blocker; CCB: Calcium Channel Blocker

There was no significant difference (P>0.05) found between numbers of antihypertensive medication prescribed in both groups (patients of with or without reduced renal function) except beta blockers. Beta blocker was more commonly prescribed to patients with reduced renal function. (p=0.005) [Table 3]

There was no statistically significant correlation found between patterns of use various antihypertensive medication and various physiological parameters like serum creatinine levels, GFR, RBS etc. (p>0.05) [Table 4]

Recommended target Blood pressure of ≤ 130/80 was achieved in 28 (56%) patients. BP control was achieved in 24 out of 38 (63.15%) in

Table-3: Patterns of Use of Antihypertensive Drugs among Patients with and without Reduced Renal Function

Drug Class	Patients Without Reduced Renal Function			Patients With Reduced Renal Function				p* value
	1 Drug N (%)	2 Drugs N (%)	Total N (%)	1 Drug N (%)	2 Drugs N (%)	3 Drugs N (%)	Total N (%)	
ACEIs	10 (100)	0	10 (100)	6 (100)	0	0	6 (100)	0.93
ARB	7 (63.63)	4 (37.37)	11 (100)	2 (66.66)	0	1 (33.33)	3 (100)	0.14
CCB	2 (33.33)	4 (66.66)	6 (100)	2 (33.33)	4 (66.66)	0	6 (100)	0.28
Thiazide	2 (28.57)	5 (71.23)	7 (100)	0	0	1 (100)	1 (100)	0.08
β Blocker	1 (50)	1 (50)	2 (100)	4 (50)	4 (50)	0	8 (100)	**0.005***
Combined α and β Blocker	2 (100)	0	2 (100)	0	0	1 (100)	1 (100)	0.62

* Chi-square test (p value <0.05 was considered significant); ACEIs: Angiotensin Converting Enzyme Inhibitors; ARB: Angiotensin Receptor Blocker; CCB: Calcium Channel Blocker

Table-4: Patterns of Utilization of Different Antihypertensive Groups and its Correlation with Physiological Parameters (n=50)

Parameters		Antihypertensive Drug Groups						p value*
		ACEIs N (%)	ARBs N (%)	Diuretics N (%)	β Blockers N (%)	CCBs N (%)	Combined α & β Blocker N (%)	
SBP (mmHg)	≤ 130	12 (75)	7 (50)	4 (50)	5 (50)	6 (50)	0	0.38
	> 130	4 (25)	7 (50)	4 (50)	5 (50)	6 (50)	3 (100)	
DBP (mmHg)	≤ 80	12 (75)	8 (57.14)	6 (75)	5 (50)	5 (41.66)	0	0.13
	> 80	4 (25)	6 (42.85)	2 (25)	5 (50)	7 (58.33)	3 (100)	
GFR (ml/min)	≥ 90	10 (62.5)	9 (64.28)	6 (75)	4 (40)	7 (58.33)	2 (66.66)	0.75
	< 90	6 (37.5)	5 (35.71)	2 (25)	6 (60)	5 (41.66)	1 (33.33)	
RBS (mg/dl)	≤ 200	12 (75)	9 (64.28)	3 (37.5)	8 (80)	8 (66.66)	0	0.26
	> 200	4 (25)	5 (35.71)	5 (62.5)	2 (20)	4 (33.33)	3 (100)	

* Chi-square test (p value <0.05 was considered significant); SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; GFR: Glomerular Filtration Rate; RBS: Random Blood Sugar; ACEIs: Angiotensin Converting Enzyme Inhibitors; ARB: Angiotensin Receptor Blocker; CCB: Calcium Channel Blocker

Table-5: Blood Pressure Control Achieved (n=50)

Blood Pressure Control		Renal Function		p value*
		Without Reduced	With Reduced	
SBP	Achieved	22	8	**0.04**
	Not achieved	9	11	
DBP	Achieved	24	6	**0.001**
	Not achieved	7	13	

* Chi-square test, p < 0.05 was considered significant

monotherapy group and in 4 out of 12 (33.33%) in polytherapy group. There was no significant difference found in control of blood pressure with regard to various antihypertensive drug classes in both group (p>0.05). However the control of systolic and diastolic blood pressure was significantly higher in patients without reduced renal function than patients with reduced renal function. (p=0.04 and p=0.001, respectively) [Table 5]

Out of total 50 patient, 9 (18%) were prescribed fixed dose combination (FDCs). Most common prescribed combination were amlodipine/ atenolol in strength of 5/50 mg and losartan/hydrochlorthiazide 50/ 12.5 mg each of which was given to 4 (44.44%) out of 9 patients. Only 1 patient was given metoprolol/amlodipine combination. Multi drug therapy was given to total 11 (22%) patients. Most common combination was CCB + beta blocker (5 patients), followed by ARB + Diuretic (3 patients), CCB + Diuretic (2 patients), ARB + CCB and ARB + Diuretic + combined alpha and beta blocker (1 patient each). The prescription of multi drug therapy did not differ significantly among patients with or without reduced renal function (P>0.05).

Discussion

This study investigated the patterns of anti-hypertensive drug therapy in diabetic-hypertensive patients with and without renal impairment. This study showed that one-third (19, 38%) of the total patients had reduced renal function (GFR< 60 mL/min) suggesting that screening for renal function among diabetic hypertensive patients and implementing rigorous therapy is important to delay progression to complications like end stage renal disease (ESRD).

This study revealed that 76% of the total patients were on single drug therapy, 22% were on two drugs, 2% were on three drugs therapy which

differs from study done by Johnson et al where monotherapy was prescribed to 23.7%, 2 drugs were given to 24%, 3 and 4 drugs 18% and 15.2% of patients respectively.[10] Our patients were overall prescribed less antihypertensive medicines than western population.

ACE-I/ARB was the most commonly prescribed drug class both in mono and combination therapy. The reported mono and combination use of ACE-I was 47.61% which is lower than that reported by Johnson et al in treating diabetic-hypertensive patients.[10] ACE-I prevents microvascular complications and can prevent progression of renal damage and also ESRD in addition to lowering BP.[7] Thus our practice coincides very well with evidence base JNC 7th guideline.

CCBs ranked second followed by beta blocker and diuretics when considering overall utilization of various anti-hypertensive drugs which differs from results of study done by Johnson et al where thiazide was second most frequently prescribed drug followed by CCBs and beta blocker.[10]The study done by Sweileh et al also showed similar utilization pattern considering overall utilization various classes.[11]

The prescription of multi drug therapy did not differ significantly among patients with or without reduced renal function. This is not in agreement with the JNC recommendation which emphasizes the role of combination therapy in this particular category of patients to delay progression to ESRD. Most commonly prescribed combinations were CCB with Beta blocker and ACE-I with diuretic. In combination of CCB and beta blocker, amlodipine was prescribed CCB along with atenolol as a beta-blocker. The combination of this drug provides added advantage because of both drugs have a different mechanism of action for reduction in blood pressure. They are also beneficial in nullifying adverse effects of each other as tachycardia caused by beta blocker is counteract by beta blockers.[12] ACE-I and thiazide combination is pharmacologically favourable since it produces an additive anti-hypertensive effect and minimizes most adverse effects of either the ACE-I or the diuretics, especially hypokalemia.[13] Even guidelines also suggests that patient with chronic kidney disease should receive ACE-I/ARB in combination with diuretic.[7] The importance of the diuretic agent was also emphasized by the "Anti-hypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial", ALLHAT study.[14]

There was no significant difference found in use of various antihypertensive drug class ($p>0.05$) in both the group, except patients with reduced renal function were more frequently prescribed beta blocker than patients without reduced renal function ($p<0.001$). In this study beta blockers were third most common group prescribed which is not coinciding with other studies Johnson et al in USA and Sweileh WM et al in Palestine.[10,11] This suggests that there is a scope for improvement in prescribing in diabetic hypertensive patients in Indian set up. The reason for more use of beta blockers in patients with reduced renal function in this study needs further evaluation.

This study also showed that there was significant difference in control of systolic as well diastolic blood pressure in patients without reduced renal function than in patients with reduced renal function. Better blood pressure control in this group is might be due to their good kidney function.

It is most important to achieve recommended blood pressure control in diabetic hypertensive patient with renal impairment. Many studies have shown to achieve this control in accordance to guidelines of JNC 7 with use of different anti-hypertensive medications in combination. Similar studies conducted by a research group Khaja et al at Bahrain on patients with type-2 DM and HTN showed that the prescribing patterns of anti-hypertensive medications differ in many instances from the World Health Organization guidelines especially, regarding the choices and drug combinations of anti-hypertensive drugs.[15]

This study has certain limitations like patients were not followed up for the gathering detailed and long term information on BP control achieved and occurrence of complications. Moreover the sample size was also small though adequate by calculation of prevalence. Larger studies involving different age groups and large number of patients

are required to implement these findings to general population of India.

This study has provided a snapshot insight into actual use of antihypertensive medicines in patients with diabetes with regard to their renal function. We conclude from this study that there was a suboptimum use of combination therapy among diabetic-hypertensive patients in general. Furthermore, diabetic-hypertensive patients with renal impairment were not given intensive anti-hypertensive therapy compared to patients with normal renal function as reflected by control achieved in systolic and diastolic BP. We recommend efficient drug use in this special group of patients. Education of health-care providers regarding appropriate and rational use of antihypertensive can help in better management of these patients. There is also a need to form guidelines at national and state level for management of these patients.

Conclusion

There was suboptimum use of combination therapy among diabetic-hypertensive patients in general and specifically in developing countries as reflected by control achieved in systolic and diastolic BP which requires concern of all healthcare professionals.

References

1. Arauz-pacheco C. The treatment of hypertension in adult patients with diabetes. Diabetes Care. January 2002;25(1):134-147.
2. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. UK prospective diabetes study group. BMJ 1998:703–13.
3. Chin MH, Su AW, Jin L, Nerney MP. Variations in the care of elderly persons with diabetes among endocrinologists, general internists, and geriatricians. J Gerontol A Biol Sci Med Sci. 2000;M601–6.
4. Harris MI. Health care and health status and outcomes for patients with type 2 diabetes. Diabetes Care. 2000;754–8.
5. Martin TL, Selby JV, Zhang D. Physician and patient prevention practices in NIDDM in a large urban managed-care organization. Diabetes Care. 1995;1124–32.
6. Chobanian AV. 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.
7. Seventh report of the Joint National committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension 2003;42(6): 1206-52.
8. Mahajan BK. Sampling. Methods in Biostatistics. 7th ed. India: Jaypee Brothers Medical Publishers; 2010. p84
9. Harrison. Chronic Kidney Disease. In: Dr. Fauci's and Dr. Longo's (eds.)Harrison's Principles Internal Medicine. 18th ed. United States: The McGraw-Hill Companies; 2008. p 2308-2321.
10. Johnson ML, Hardeep Singh. Patterns of Antihypertensive Therapy Among Patients with Diabetes. Journal of General Internal Medicine.2005;20(9):842–846.
11. Sweileh WM, Sawalha AF, Zyoud SH, Al-Jabil SW, Tameem EJ, Shraim NY. Evaluation of antihypertensive therapy in diabetic hypertensive patients: impact of ischemic heart disease. Pharmacy Practice (Internet) 2009 Jan-Mar;7(1):40-46.
12. Harrison. Hypertensive Vascular Disease. In: Dr. Fauci's and Dr. Longo's (eds.)Harrison's Principles Internal Medicine. 18th ed. United States: The McGraw-Hill Companies; 2008. p 2042-2059.
13. Ishimitsu T, Yagi S, Ebihara A, Doi Y, Domae A, Shibata A. Long term evaluation of combined antihypertensive therapy with lisinopril and a thiazide diuretic in patients with essential hypertension. Jpn Heart J 1997;38:831- 40.
14. Major outcomes in high risk hypertensive patients randomized to angiotensin-converting enzyme inhibitors or calcium channel blockers vs diuretics: The antihypertensive and Lipid- Lowering Treatment to prevent Heart Attack Trial (ALLHAT). JAMA 2002; 288:2981-97.
15. Al Khaja KA, Sequeira RP, Mathur VS, Damanhori AH, Abdul Wahab AW. Family physicians' and general practitioners' approaches to drug management of diabetic hypertension in primary care. J Eval Clin Pract 2002;8(1):19-30.

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