

Research Article

Antihypertensive drug utilization pattern and awareness in diabetic hypertensive patients at tertiary care centre

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ABSTRACT

Background: Patients with diabetes has 2 fold higher chances of suffering from hypertension. Hypertension is risk factor for development of diabetes as well for complications like nephropathy, CAD and neuropathy etc. Hypertension control is vital to prevent and retard progression of microvascular and macrovascular complications. Therefore, we undertook this study to evaluate treatment patterns in diabetic patients with hypertension, those are being followed at our institute.

Methods: Study group comprised of diabetic patients who had hypertension as well. All patients with diabetes reporting to medicine OPD from March 2014 to September 2014 at our institute were screened. Patients with follow up of at least 3 months and age more than 18 years of either sex were included.

Results: There were 223 patients. Study group comprised of 121 males and 102 females. Mean age of group was 48.6 years. One hundred three patients (46.18%) were on monotherapy and remaining 120 patients were on combination antihypertensive drugs. There were total 398 antihypertensive drug exposures. Patient needed mean antihypertensive drug of 1.78. Angiotensin receptor blockers were the most commonly prescribed drugs. Angiotensin inhibitors (angiotensin receptor blockers and ACE inhibitors) were utilized in 158 (71%) patients. Hypertension control was achieved in 84 (37.66%) patients. One hundred eighty one patients (81.2%) knew about disease.

Conclusion: Our study showed that majority of diabetic hypertensive patients needed multiple drug therapy to control hypertension. Most of the patients were on ARBs/ACE inhibitors. This was according to recommendation by ADA or JNC8.

Keywords: Diabetes, Hypertension, Antihypertensive drugs, Angiotensin receptor blocker

INTRODUCTION

Hypertension and Diabetes are life style disease and are the major burden of global Health due to complications. India currently has 40.9 million diabetic patients and it is expected to rise to 69.9 million by 2025 unless urgent and effective preventive steps are taken.¹ One and half billion people will suffer from hypertension² and 300 million will suffer from diabetes by 2025.³ Prevalence of hypertension is 60% in type 2

DM.⁴ Patients with T2DM has two fold higher chances of suffering from hypertension in comparison to age match subjects without diabetes.⁵ Hypertension has been shown as a major risk factor not only for the development of diabetes but also for the development of micro and macro vascular complications like neuropathy, nephropathy, retinopathy, coronary artery disease, stroke, Peripheral Vascular Disease (PVD) in diabetic patients. The benefits of Blood Pressure (BP) control in diabetic patients exceed the benefits of tight glycemic control and vital to the

prevent and retard progression of both microvascular and macrovascular complications of hyperglycemias.⁶ Therefore, all of the hypertension management guidelines, that is, eighth report of Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure-2013 (JNC-8),⁷ American Diabetes association (ADA) 2014⁸ and European Society of Hypertension (ESH 2013)⁹ focused aggressively on Blood Pressure (BP) control in diabetic patient to below 140/80-90 mmHg. JNC 8 recommended target of diastolic BP <90 mmHg and ESC 2013 recommended <85 mmHg. But ADA recommended target of DBP <80 mmHg. There are limited data from India regarding physician's choices of anti-hypertensive therapies for a patient with diabetes in single- and multiple-drug based regimens. Therefore, we undertook this study to evaluate treatment patterns in diabetic patients with hypertension, those are being followed at our institute. Our objectives were:

1. To evaluate the utilization of ACEI or Angiotensin Receptor Blockers (ARBs) and other preferred anti-hypertensive therapies based on the JNC VIII guidelines as agents to treat diabetic hypertension,
2. To compare utilization of different types of antihypertensive therapies in other comorbid conditions
3. To assess BP control in this population.
4. To assess awareness about hypertension in the study group.

METHODS

Our study group comprised of diabetic patients who had hypertension as well. All patients with diabetes reporting to medicine OPD from March 2014 to September 2014 at our institute were screened. Inclusion criteria-

1. Patients with age > 18 years of either sex
2. Follow up of at least 3 months.
3. Patients with diabetes and hypertension both.

Patients with advance renal failure (serum creatinine >3.5 mg%) and patients with malignant hypertension were excluded. Patients were diagnosed hypertensive if they had at least 2 visits with diagnosis of hypertension or they had prescription of antihypertensive drug with one recording of elevated BP or they had elevated BP on two visits. Elevated BP was defined as systolic BP >139 mmHg and Diastolic BP (DBP) >89 mmHg.⁷ Patients were diagnosed as diabetic if they had two visits with diagnosed of diabetes or they had prescription of antidiabetic drugs or insulin or raised glycosylated hemoglobin. All basic demographic information in form of age sex, diagnosis, and duration of diabetes was

recorded. Any comorbidity like nephropathy, neuropathy, Coronary Artery Disease (CAD), stroke or retinopathy were recorded. Patients were diagnosed nephropathy if urine showed proteinuria on 2 occasions or estimated Glomerular Filtration Rate (eGFR) was <60 ml/minute. Creatinine clearance and GFR were calculated from the serum creatinine levels using a Cockcroft-Gault equation.¹⁰ Their basic investigations like complete blood count, renal function test, fasting and post prandial plasma glucose level, fasting serum lipid profile was recorded. Patients also underwent ECG and fundus examination.

Patients were diagnosed with CAD if they had symptoms suggestive of CAD with ECG evidence or echocardiographic evidence or positive treadmill test or evidence in coronary arteriography. Data of antihypertensive drugs was recorded and grouped according to class of drug. Antihypertensive drugs were grouped in to seven groups - Calcium channel blockers, beta blockers, diuretics, Alfa blockers, Angiotensin Convertase Enzyme Inhibitors (ACEI), Angiotensin Receptor Blockers (ARB), centrally acting drugs. Data for antihypertensive drugs was recorded in form of need of monotherapy, two drugs or three drugs therapy. Data for non-pharmacological therapy was also recorded like salt restriction, loss of weight or exercise. Patients were asked about if they know about hypertension, complication or control of hypertension. They were asked if they knew about systolic or diastolic hypertension. Data was analyzed by SPSS 1.7 version. Data was recorded as mean ± standard deviation. P value of <0.05 was considered significant.

RESULTS

There were 223 patients in this study. Our study group comprised of 121 males and 102 females. Gender ratio of study group was 1.18:1(males: females). Mean age of the cohort was 48.6 ± 7.8 (18-86 years) years. Patients had mean duration of diabetes of 4.2 ± 2.9 years. Demographic data of patients has been described in Table 1. Patients had various comorbidities in form of nephropathy, Coronary Artery Disease (CAD), retinopathy and dyslipidemia. These comorbidities have been shown in Table 2. One hundred three patients (46.18%) were on monotherapy and remaining 120 patients were on combination antihypertensive drugs. There were total 398 antihypertensive drug exposures. Patient needed mean antihypertensive drug of 1.78.

Number of drugs - Monotherapy was needed in 46.18% (n =103) patients and dual therapy was required in 32.73% (n=73) patients. Thirty nine patients (17.48%) were on triple drug therapy and eight patients (8.07%) were on quadruple drug therapy.

Type of drug - Angiotensin receptor blockers were the most commonly prescribed drugs. Angiotensin inhibitors (angiotensin receptor blockers and ACE inhibitors) were

utilized in 158 (71%) patients. These were followed by calcium channel blockers, diuretics, and beta blockers.

Table 3 describes relative frequency of utilization of different antihypertensive drugs.

Table 1: Showing epidemiology data.

Age (years)	Number	Percentage	Male	Female	Monotherapy	Dual therapy	Triple therapy	Quadruple therapy
<35	28	12.55	19	9	12	13	3	0
35-50	83	36.77	45	38	41	26	13	3
50-75	91	40.80	46	45	40	28	19	4
>75	21	9.41	11	10	10	6	4	1
Total	223	100	121	102	103	73	39	8

Table 2: Showing comorbidity.

Comorbidity	Number	Percentage
Retinopathy	104	46.63
Nephropathy	65	29.14
Neuropathy	64	29
CAD	47	21.09
PVD	27	12.10

CAD-Coronary artery disease, PVD-Peripheral vascular disease

Table 3: Showing utilization of various drugs.

Drug	Number of patients	Percentage
Angiotensin receptor blocker	99	44.39
Calcium channel blocker	84	37.66
Diuretic	78	34.97
ACE inhibitor	59	26.45
Beta blocker	58	26
Alfa blocker	12	5.38
Central agonist	8	3.58

Combination Utilization pattern - Angiotensin receptor blocker with diuretics was the most commonly used dual drug combination strategy in our study. It was followed by combination of beta blocker with calcium channel blocker, calcium channel blocker with angiotensin receptor blocker, ACE inhibitor with diuretic and ACE inhibitor with beta blocker. Combination utilization pattern has been shown in Table 4. Combination of Beta blocker with calcium channel blocker and diuretic was most commonly (51.28%) used in patients on triple drug combination. Combination of ARB, diuretic with CCB was used in 33.3% (n=13) and combination of Alfa blocker, BB and diuretic was used in 10.24% (n=4). Combination of ACEI, CCB with diuretic was used in 5.12% (n=2) patients. Combination of ACEI/ARB, diuretic with centrally acting drugs was used in 15.9% (n=7) patients.

Table 4: Description of combination utilization (Dual drug).

Drug combination	Number	Percentage
ARB+D	22	30.13
CCB+BB	15	20.55
ARB+CCB	14	19.17
ACEI+D	12	16.43
ACEI+BB	10	13.69
Total	73	100

ARB-Angiotensin receptor blocker, D-Diuretic, CCB-Calcium channel blocker, BB-Beta blocker, ACEI-ACE inhibitor

Majority patients (50%) on quadruple therapy were on combination of Alfa blocker, diuretic, ACE inhibitor and central agonist. Combination of Alfa blocker, diuretic, central agonist with CCB or ARB was used in remaining 50% patients.

Choice of drug according to comorbidity - There were 65 patients with diabetic nephropathy. They had total 132 antihypertensive drug exposure. They needed mean antihypertensive drug intake of 2.03. Monotherapy was needed in 27.69% (n=18) patients. Dual drug combination was used in 47.69% (n=31) and triple drug combination was used in 18.46% (n=12) patients. Quadruple drug therapy was utilized in 6.15% (n=4) patients. Angiotensin based therapy (ARB or ACE inhibitors) were used in majority (81.53%) of patients. These were followed by diuretic (49.23%), calcium channel blocker (41.53%), Beta blocker (18.46%), alfa blocker (6.15%) and central agonist (6.15%).

There were 47 patients with CAD. Fifteen patients (31.91%) were on monotherapy. Dual drug combination was used in 53.19% (n=25) patients. Triple drug combination was used in 14.89% (n=7) patients. No patient was on quadruple therapy. Forty one patients (87.23%) were on Beta blockers. Calcium channel blockers were used in 28 (59.57%) and ACE inhibitors

were used in 10 (21.27%) patients. Diuretics were used in 7 patients.

Use of non-pharmacological therapy - Life style modification in form of salt restriction, exercise, weight loss and other dietary therapy was advised to 185 (82.95%) patients.

Awareness about hypertension - One hundred eighty one patients (81.2%) knew about disease. Only 116 (52%) patients knew about systolic and diastolic pressure. There was awareness in 86 patients (38.56%) about target blood pressure.

Control of hypertension - Hypertension control was achieved in 84 (37.66%) patients. BP control was taken as office BP recording of <140/90 mmHg. Sixteen patients with diabetic nephropathy had office BP recording of <140/90 mmHg. Patients with diabetic nephropathy had lesser chance of BP control in comparison to patients without diabetic nephropathy. Z score was 2.580 and P = 0.0098.

Usage of different antihypertensive in different population - Usage of ACEI and ARB was significantly higher in patients with diabetic nephropathy in comparison to patients without diabetic nephropathy. Z score was 2.7892 and P was <0.05. Patients with CAD had significantly higher usage of Beta blockers. Z score was 10.77 and P was <0.05.

DISCUSSION

Our study tried to find utilization of various antihypertensive drugs in diabetic hypertensive patients and awareness about hypertension. A prescription based study is an effective way to assess and evaluate prescribing altitude of physicians.¹¹ Majority of patients in our study were on multidrug regimens. Only 46% patients were on single drug therapy. It is consistent with other studies.^{12,13} Berlowitz et al.¹⁴ have shown worse BP control in patients with diabetes and less intensive anti-hypertensive medication therapy. ARB was the most common drug prescribed in 44.39% patients either alone or in combination. ACEI/ARB were used in 158 (71%) patients either alone or in combination. Most of the patients (76.6%) on single drug were receiving either ACEI or ARB. There is suggestion that ARBs should be a regular component of combination treatment and preferred drug in patients on monotherapy in diabetics.¹⁵ It has been described that initial monotherapy ACE inhibitors may be superior to dihydropyridine CCB in reducing cardiovascular events.^{16,17} Calcium channel blockers were used in 37.66% patients either in combination or as monotherapy. JNC 8 also recommends calcium channel blockers as first line drug in diabetic hypertensive patient.⁷ CCBs ranked second followed by diuretics when considering overall utilization pattern of various anti-hypertensive drugs but Johnson et al found thiazide was second most frequently prescribed drug

followed by CCBs and beta blocker. CCBs ranked second followed by diuretics when considering overall utilization pattern of various anti-hypertensive drugs in Indian study.¹⁸ Diuretics were used in 34% patients either as single or combination therapy. Diuretic use ranked third after CCBs and these were more commonly used as part of multidrug regimen. Dhanraj et al. described same pattern in their study on diabetic hypertensives.¹⁹ Beta Blockers were used in 26% patients. Usage of BB was significantly higher in patients with CAD in our study. BB has protective effect in CAD and other studies^{19,20} also found higher use of BB in patients with CAD.

ARB/ACEI with diuretic was the most commonly used combination therapy. It is consistent with other study. Patients with nephropathy needed higher no of antihypertensive drugs. Use of ACEI/ARB was higher in patients with nephropathy than without nephropathy. Shah et al.¹⁸ also found similar pattern in their patients. Use of ACEI and ARB has been recommended by ADA⁹ also. Blood pressure control was achieved in 37.66% patients. Our control rates are better than other studies^{19,22} with control rate of 25-32%. Which may be due to difference in sample size. Patients with nephropathy had lesser percentage of patients with control of hypertension than patients without nephropathy. Shah et al¹⁸ also described similar pattern. Awareness about hypertension was found in 81% patients. Asfaq et al. also found awareness in 80% patients attending tertiary care hospital.²³

CONCLUSION

Our study showed that majority of diabetic hypertensive patients needed multiple drug therapy to control hypertension. Most of the patients were on ARBs/ACE inhibitors. This was according to recommendation by ADA or JNC8. Patients with diabetes had lesser chance of control of hypertension. Hypertension control was achieved in 37% patients. We found awareness rate of 81% in our study group. Still there is room for better control of hypertension and optimization of antihypertensive therapy.

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Ethical approval: The study was approved by the institutional ethics committee

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