

Usage of diuretics among diabetic-hypertensive patients

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ABSTRACT

Background: Hypertension is more common in diabetics than in non-diabetic patients. An aggressive approach to the diagnosis and treatment of hypertension in patients with diabetes is required in order to substantially reduce the incidence of both macro-vascular and micro-vascular complications. The role of diuretics in the treatment of hypertension as first line or second line drugs is a provoking debate, hence we studied the usage of diuretics and their effects on BP and glycemic control among diabetic-hypertensive patients. **Methods:** This cross sectional study was carried out for a period of six months in a tertiary care teaching hospital. Patients' details such as age, gender, height, weight, comorbid diseases, blood pressure, eGFR along with duration of diabetes and hypertension and drugs prescribed for hypertension were noted. Data were analyzed using descriptive statistics. **Results:** A total of 336 diabetic-hypertensives with a mean age of 64.55 ± 9.51 years were included. Fortyfive patients were on diuretics, two (4.4%) of whom were on diuretic monotherapy, 16 (35.6%) on two drug combinations (Diuretic + ACEI or ARB), 21 (46.7%) on three drug combinations (diuretics + ARB & BBs or diuretic + ACEI & BB or diuretic + ARB & CCB) and six (13.3%) were on four drug combinations (diuretics + ARB, CCB & BB). Among the patients on diuretic combination therapy BP was well controlled in 23 (51%) patients and the glycemic control was comparable to those not on diuretics. **Conclusion:** In the present study the usage of diuretics was consistent with the guidelines. About 13% of diabetic-hypertensive patients were on diuretic treatment. The control of BP in patients on diuretics was not satisfactory, but there was no worsening of glycemic control compared to other antihypertensive therapy. This shows that low dose thiazides in combination with other antihypertensives can be safe in diabetic-hypertensive patients however their efficacy needs further scrutiny.

Keywords: Diabetes mellitus, Diuretics, Hypertension, Thiazides

INTRODUCTION

Hypertension is a common comorbid condition in diabetes; it is 1.5 to three times more common in patients with diabetes than in those without diabetes.¹ The world diabetes capital, India, in the next thirty years may also be the world hypertension capital.² Hypertension and diabetes mellitus (DM) are both important contributory factors for the growing burden of cardiovascular and chronic kidney disease.³ Achieving the recommended goal of blood pressure (< 130/80 mm Hg) in hypertensives with DM is difficult in a majority of patients.^{4,5} An aggressive approach to the diagnosis and treatment of hypertension in patients

with diabetes is required in order to substantially reduce the incidence of both macro-vascular and micro-vascular complications. The anti-hypertensive agents used in diabetic patients should not only aim at controlling hypertension but also at preventing/delaying the development of complications.⁶ Several factors are important in selecting anti-hypertensive agents for diabetic-hypertensive patients.

Guidelines for the treatment of hypertension recommend that thiazide diuretics should be the preferred drugs in most hypertensive patients, including in diabetics, either alone or combined with drugs from other classes.⁷ Diuretics have been used effectively to treat hypertensive patients

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in the past four decades. Although thiazide and thiazide-like diuretics are indispensable drugs in the treatment of hypertension, their role as first-line or even second-line drugs among diabetics is a provoking debate.⁸ Recently diuretics received less enthusiasm compared with newer agents, and their role in the treatment of diabetic patients has been scrutinized due to the potential for adverse effects on glucose and lipid levels and the physiologic response to hypoglycemia.⁹ Hence this study was undertaken to analyse the usage of diuretics and their effects on BP and glycemic control among diabetic-hypertensive patients.

MATERIALS AND METHODS

This cross sectional study was carried out for a period of six months in a tertiary care teaching hospital. Patients with both diabetes and hypertension were included in the study after getting approval from the institutional ethics committee and obtaining a written informed consent from the patients. Patients' details such as age, gender, height, weight, comorbid diseases, blood pressure [Systolic blood pressure (SBP), Diastolic blood pressure (DBP)], eGFR along with duration of diabetes and hypertension and drugs prescribed for hypertension were noted on a proforma. Data were analyzed using descriptive statistics.

RESULTS

A total of 336 diabetic patients with hypertension were included in the study, 163 (48.5%) were males & 173 (51.5%) were females. The mean age of the study population was 64.55±9.51 years. Table 1 shows the demographic and clinical data of the study population.

Among the 336 diabetic-hypertensive patients, 45(13.4%) were on diuretics. The diuretics used by them were hydrochlorothiazide (45 patients), furosemide (28 patients) and spironolactone (23 patients). Diuretics were used in combination with other antihypertensive groups like ARBs, ACEIs, BB and CCB. Out of the 45 patients on diuretics two patients (4.4%) were on diuretic monotherapy, 16 patients (35.6%) were on two drug combinations, 21 patients (46.7%) were on three drug combinations and

six patients (13.3%) were on four drug combinations. In two drug combinations along with diuretics ACEIs were prescribed the most, followed by ARBs. In three drug combinations along with diuretics ARBs plus BBs were highest followed by ACEIs plus BBs and ARBs plus CCBs. In four drug combination diuretics with ARB, CCB & BBs were commonly prescribed (Table 2).

Among the ARBs losartan and telmisartan; among the ACEIs enalapril and ramipril; among the beta blockers atenolol and metoprolol and among the CCBs amlodipine were the agents used. Commonly used antihypertensive agents along with diuretics were losartan (17 patients), amlodipine (16 patients) and enalapril (13 patients).

The comorbidities that were present in the 45 patients on diuretics were dyslipidemia (14 patients), ischemic heart disease (12 patients), peripheral neuropathy (13 patients), nephropathy (4 patients), cerebrovascular accident and retinopathy (3 patients).

Table 3 shows the effects of diuretic combination therapy and other antihypertensive therapy on blood pressure and glycemic control. Among the 45 patients who were on diuretics, the blood pressure was well controlled

Table 1: Demographic and clinical data of diabetic-hypertensive patients

Characteristics	Mean±SD (N=336)
Age (years)	64.55±9.51
Duration of DM (years)	10.83±8.74
Duration of HTN (years)	7.39±6.91
SBP (mmHg)	138.17±13.11
DBP (mmHg)	82.05±6.17

Table 2: Prescribing pattern of diuretics with other antihypertensive drug groups

Drug combination	N=45 (%)
Diuretics alone	2 (4.44)
2 drug combinations	
Diuretic+BBs	1 (2.22)
Diuretic+CCBs	1 (2.22)
Diuretic+ARBs	6 (13.33)
Diuretic+ACEIs	8 (17.77)
3 drug Combinations	
Diuretic+ACEIs+BBs	5 (11.11)
Diuretic+ACEIs+CCBs	4 (8.88)
Diuretic+ACEIs+ARBs	1 (2.22)
Diuretic+ARBs+BBs	6 (13.33)
Diuretic+ARBs+CCBs	5 (11.11)
4 drug Combinations	
Diuretic+ARBs+CCBs+BBs	4 (8.88)
Diuretic+ACEIs+ARBs+CCB	1 (2.22)
Diuretic+ACEIs+CCBs+BBs	1 (2.22)

Table 3: Effects of antihypertensive combination therapy on blood pressure and glycemic control

Drug therapy	Controlled (N) (%)	Not controlled (N) (%)
Blood pressure		
Diuretic combination therapy (N=45)	23 (51)	22 (49)
Other antihypertensive therapy (N=291)	217 (75)	74 (25)
Glycemic Control		
Diuretic combination therapy (N=45)	18 (40)	27 (60)
Other antihypertensive therapy (N=291)	117 (40)	174 (60)

($\leq 140/90$ mm of Hg) in 23 (51%) patients and there was a good glycemic control ($\text{HbA}_{1\text{C}} < 7$) in 18 (40%) patients.

DISCUSSION

Diuretics are used in hypertension because of their efficacy, low cost, synergistic effect when used in combination with other antihypertensive agents and the fact that they counteract salt and fluid retention caused by other antihypertensive agents; and, also their beneficial effects in patients with heart failure. Thiazide diuretics are the first choice of agents in non-diabetic patients, but there has been a tendency to avoid their use in patients with diabetes due to concerns over adverse metabolic effects, despite evidence that these are minimal when lower doses are used.¹⁰ High-dose diuretics have detrimental effects on glycemic control as well as on triglyceride and cholesterol.¹¹ Hence low-dose diuretics are now more commonly prescribed. Low-dose diuretics are noted to augment the anti-hypertensive effects of other major groups of antihypertensive agents and therefore work well in combinations.¹² In a previous study diuretics were prescribed in 28% of diabetic hypertensive patients.¹³ In our study only 13.4% (45 patients) of the diabetic-hypertensive patients were on thiazides which were prescribed in low dose (hydrochlorothiazide 6.25 to 25 mg/day), probably because of the concern of adverse effect on glycemic control and hyponatremia in the elderly. Among those 45 patients, only two patients were on monotherapy whereas all others were on low dose of diuretics in combination with other antihypertensive agents. The $\text{HbA}_{1\text{C}}$ of the two patients on diuretic monotherapy was 7 & 7.7% and the mean $\text{HbA}_{1\text{C}}$ of all the patients on diuretics was $7.7 \pm 1.41\%$, which was satisfactory.¹⁴ The glycemic control was similar in both the study groups (i.e. patients on diuretic combination therapy and patients not on diuretics). Among the 45 patients on diuretics, 18 (40%) had $\text{HbA}_{1\text{C}} < 7$, while 117 (40%) patients not on diuretics had $\text{HbA}_{1\text{C}} < 7$, which is considered as well-controlled.¹⁴ Hence thiazides in low doses can be safely used in diabetic hypertensive without much change in the glycemic control.

Current antihypertensive guidelines recommend BP goal for diabetic patients as $< 140/90$ mmHg.⁷ In the present study in 22 (49%) patients receiving diuretic combination therapy and in 74 (25%) patients who were not on diuretics, this recommended goal of BP was not met. This shows that use of low dose diuretics may not be very efficacious in controlling hypertension, though there was no deleterious effect on the glycemic control compared to other antihypertensive agents. However, one of the limitations of this inference is that there may be other confounding factors apart from the use of diuretics which

may have affected the control of BP; but analysis of these factors was beyond the scope of our study.

There were 28 patients on furosemide. Furosemide is indicated in patients with impaired renal function. The mean eGFR of the patients on furosemide was 50.9 ± 22.12 ml/min hence furosemide may have been prescribed in these patients.

Most diabetic-hypertensive patients require more than one agent to attain adequate blood pressure control. Renin Angiotensin Aldosterone System (RAAS) inhibitor and a diuretic combination will offset the diuretic-induced increase in plasma renin activity. The salt loss will add to the antihypertensive effect of RAAS blocker. ARB will also attenuate the metabolic adverse effects (like hypokalemia and hyperglycemia) of thiazide diuretics.¹⁵ In the present study along with diuretics ARBs and ACEIs were the commonly prescribed antihypertensive groups followed by BBs and CCBs, which is in accordance with the recommended guidelines.^{4,16} The maximal use of thiazide diuretics with RAAS inhibitors is comparable to the earlier report by Ethiraj Dhanaraj et al.¹⁷ Angiotensin-converting enzyme (ACE) inhibitors prevent or delay microvascular and macrovascular complications of diabetes, delay progression of diabetic kidney disease and are recommended as first-line antihypertensive agents in patients with diabetes. ARBs may be used in patients who cannot tolerate ACE inhibitors. If adequate titration of the ACE inhibitor or ARB does not provide satisfactory blood pressure reduction, addition of a thiazide diuretic is the next step. If blood pressure is not controlled with the addition of a beta blocker, a CCB should be added.^{1,18,19} In our study the same pattern of antihypertensive use was noted which is consistent with the guidelines.

Fourteen patients (31.11%) who were on diuretic therapy had dyslipidemia. Hypertension and dyslipidemia can coexist frequently. Among the antihypertensive agents ARBs have shown to improve insulin sensitivity and reduce triglyceride levels^{20,21} and this could be one of the reasons for the higher usage of ARB in combination with diuretics in our study.

In our study along with diuretic, next to losartan, amlodipine was used the most. Controversy exists regarding the use of CCBs, particularly the dihydropyridines in treating diabetic-hypertensives. Some studies showed higher incidence of cardiac events in diabetic patients treated with dihydropyridine CCBs, as compared with ACE inhibitors.^{22,23} In other studies,²⁴⁻²⁶ the use of dihydropyridine CCBs, as monotherapy or in combination with another antihypertensive agent, was associated with a reduction in cardiovascular risk.

CONCLUSION

In the present study the usage of diuretics was consistent with the guidelines. About 13% of diabetic-hypertensive patients were on diuretic treatment. The control of BP in patients on diuretics was not satisfactory, but there was no worsening of glycemic control compared to other antihypertensive therapy. This shows that low dose thiazides in combination with other anti hypertensives can be safe in diabetic-hypertensive patients however their efficacy needs further scrutiny.

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Authors Contribution:

RS – Designed the study, analysed the data, drafted the manuscript, & reviewed the manuscript; **PAMR** – Designed the study & reviewed the manuscript; **SDU** – Analysed the data & drafted the manuscript; **SK** – Analysed the data.

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