

Comparison of Antihypertensive Combination Therapy and Glycemic Control in Diabetic Hypertensive Patients

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Abstract

Objective: To compare the glycemic level in diabetic hypertensive patients who were on antihypertensive combination therapy and to evaluate utilization patterns of antihypertensive combination therapy among diabetic hypertensive patients in a government tertiary care hospital at Erode.

Methods: The prospective observational study was undertaken at the inpatient department in a tertiary health care hospital, Erode, Tamil Nadu. The study was performed for a six months period after obtaining clearance from J.K.K. Natraja College of Pharmacy's Ethical committee. A data entry form was prepared to record patient details like name, age, sex, educational status, life events, and social history and prescribed drugs. After obtaining informed consent form from the patient, the demographic data were collected. A total of 200 cases were collected and among that 112 patients were on antihypertensive combination therapy which included diuretics, beta blockers (BB), angiotensin converting enzyme inhibitors (ACEI's), and calcium channel blockers (CCB's). The glycemic level of 112 diabetic hypertensive patients under antihypertensive combination therapy was compared by taking their FBS and RBS reading.

Result: In this study out of 200 cases collected, 56 (28%) patients were on antihypertensive mono therapy and 112 (56%) patients were on antihypertensive combination therapy and the rest of the patients didn't know the medicines that they were taking. Here, out of 112 patients 35 patients had an elevated random blood sugar (RBS) reading (above 300 mg/dl). In these 35 patients, 20 patients (58.82%) were on diuretics (furosemide) and BB (atenolol) combination therapy. Fasting blood sugar level FBS level was elevated (above 200mg/dl) in 45 patients. Wherein 26 patients (57.78 %) were on diuretics (furosemide) and BB (atenolol) combination therapy. Finally, it was observed that the patients who were on diuretic (furosemide) therapy in combination with BB (atenolol) had an elevated blood glucose level in comparison with the patients who were on other antihypertensive combination therapy.

Conclusion: The most commonly used antihypertensive 2 drug combination therapy was CCB and BB (31.25%) followed by diuretics and BB (29.46%). This study shows CCB in combination with BB as the most commonly prescribed drug therapy for treating hypertension in patients with diabetics, after tabulating the data it shows that the patients under diuretic (furosemide) therapy in combination with beta blocker (atenolol) had an elevated blood glucose level in comparison with the patients under other antihypertensive combination therapy. Further, it was also observed that the most number of patients with comparatively lesser elevation in blood sugar level was under CCB and BB (atenolol)

Keywords: Diabetes Mellitus, Antihypertensives, Hypertension, Combination therapy

1. INTRODUCTION

Diabetes and hypertension are common diseases of great importance and their management requires attention, both clinically and pharmacologically. Hypertension is extremely common co morbidity in patients with type 2 diabetes mellitus. The presence of hypertension in patients with type 2 diabetes is particularly destructive because of their strong linkage with cardiovascular diseases (CVD), stroke, progression of renal disease and diabetic nephropathy [1]. Even it is very hard to control hypertension in diabetic hypertensive patients and hence antihypertensive combination therapy is required to take control over the elevated blood pressure [2]. In type II diabetics also, hypertension and diabetes are commonly associated and here obesity is the factor which could produce a spurious association [3]. Despite these possible confounding factors, most studies which have taken obesity and nephropathy into account still report a strong association between hypertension and diabetes, although this remains a controversial point [4]. In any event, a large number of patients with both hypertension and diabetes do exist. These patients have two major risk factors for cardiovascular disease and it is important, therefore, to

establish guidelines for their management. Furthermore, we now have information that controlling blood pressure in diabetics is positively beneficial as far as the progression of nephropathy is concerned. Balanced against this, however, is the problem that most available antihypertensive drugs are known to worsen glycaemic control and we have no comparative data to guide us on which drugs we should use.

2. MATERIALS AND METHODS

The prospective observational study was undertaken at the Inpatient department in a tertiary health care hospital, Erode, Tamil Nadu. The study was performed for a period of six months. A separate data entry form was prepared to record patient details like name, age, sex, educational status, life events, social history and prescribed drugs. After obtaining informed consent form from the patient, the demographic data like (age, gender, educational status, diagnosis and prescriptions) were collected by using a suitable data entry form. Patients with hypertension, diabetes and comorbid disease were selected. The utilization pattern of antihypertensive therapy was analyzed and also the glycemic levels of patients taking

antihypertensive combination were analyzed. A total of 200 cases of both male and female sex and age group of 40-70 years were collected and among those 112 patients were on antihypertensive combination therapy. The glycemic level of 112 diabetic hypertensive patients under antihypertensive combination therapy was compared by taking their FBS and RBS reading.

3. RESULT:

Table 1: Demographic presentation of diabetic hypertensive patients by age.

Age group (in years)	Male (n=128)	Female (n=72)	Total no. of patients (n=200)
40-50	32	16	48
51-60	40	24	64
61-70	56	32	88

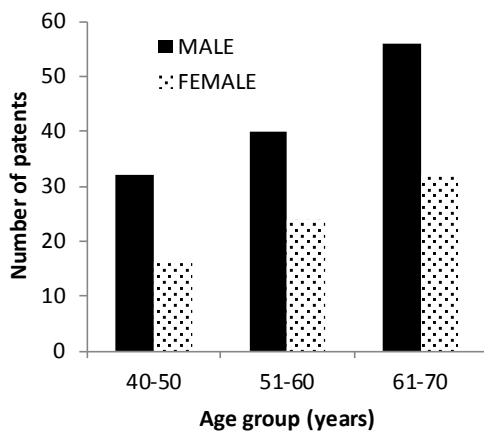


Fig. 1: Demographic presentation of diabetic hypertensive patients by age

Table 2: Co morbid diseases in diabetic hypertensive patients.

Co morbid disease (n=200)	Male (n=128)	Percentage of patients	Female (n=72)	Percentage of patients
CVA	43	33.59	28	38.88
CVD	56	43.75	20	27.77
ARF/CRF	29	22.65	24	33.33

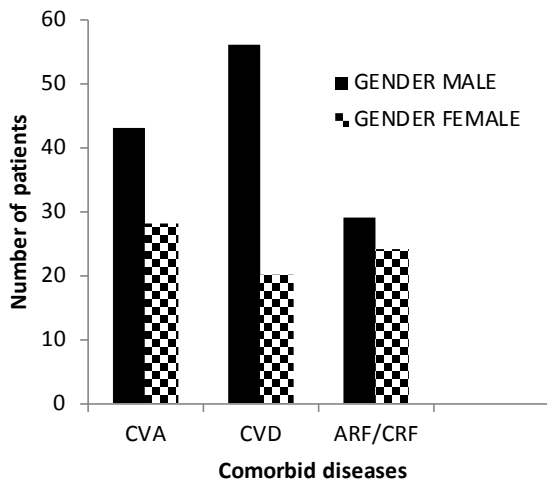


Fig. 2: Co morbid diseases in diabetic hypertensive patients.

Table 3: Drugs used in the study along with their pharmacological class.

Sl.No	Class of antihypertensive drugs	Drugs
1	Diuretics	Furosemide
2	Beta blockers	Atenolol
3	Ace inhibitors	Enalapril
4	Calcium channel blockers	Amlodipine

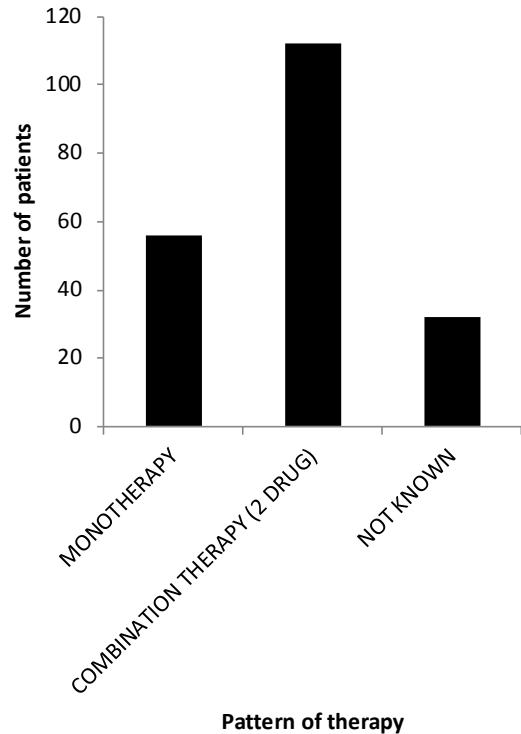


Fig. 3: Utilization pattern in diabetic hypertensive patient

Table 4: Drug utilization pattern in diabetic hypertensive patients.

Sl.no	Pattern of therapy (n=200)	Number of patients (n=200)	% of patients
1	Monotherapy	56	28%
2	Combination therapy (2 drug)	112	56%
3	Not known	32	16%

Table 5: Anti hypertensive combination drug utilization pattern in diabetic hypertensive patients

Sl.no	Antihypertensive combination therapies	No. Of patients (n=112)	Percentage(%)
1	ACE inhibitors & beta blockers	26	23.21%
2	Diuretics & beta blockers	33	29.46%
3	Calcium channel blockers & beta blockers	35	31.25%
4	Diuretics & ACE inhibitors	17	15.18%
5	ACE inhibitors & beta blockers	1	0.89%

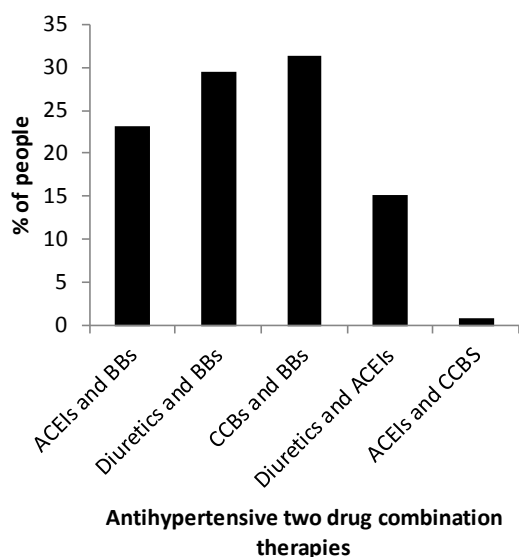


Fig. 4: Anti hypertensive combination drug utilization pattern in diabetic hypertensive patients

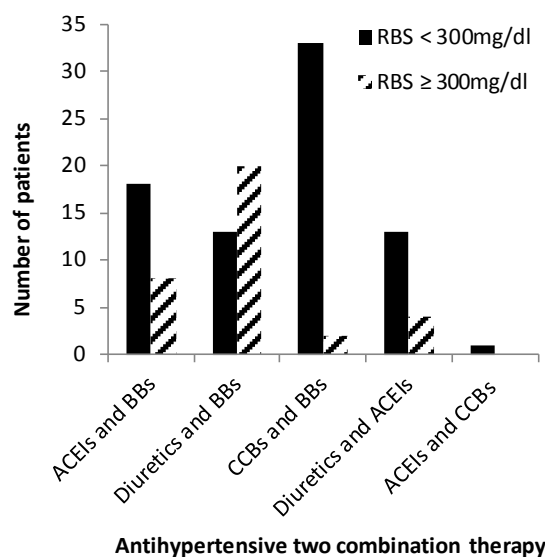


Fig. 6: Random blood sugar level in patients who have taken antihypertensive two drug combination therapy.

Table 6: Anti hypertensive combination and various clinical parameters in diabetic hypertensive patients

Sl. no	Combination therapy	RBS(n=112)		FBS(n=112)	
		<300m g/dl (n=77)	≥300m g/dl (n=35)	<200m g/dl (n=66)	≥200m g/dl (n=46)
1	ACEIs and BBs	18	8	17	9
2	Diuretics and BBs	13	20	7	26
3	CCBs and BBs	33	2	33	2
4	Diuretics and ACEIs	13	4	9	8
5	ACEIs and CCBs	1	0	1	0

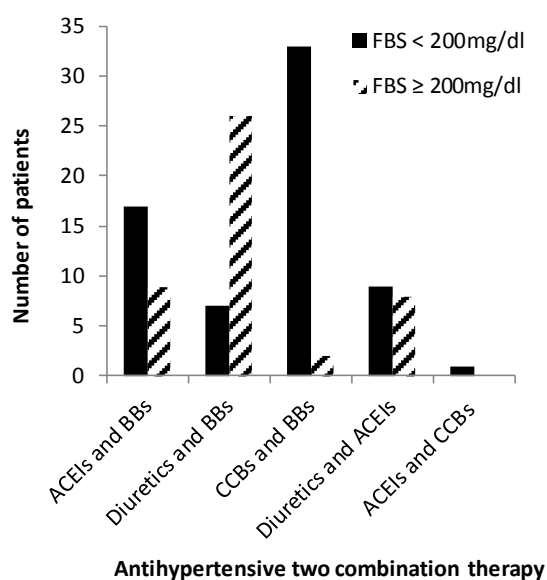


Fig. 5: Fasting blood glucose level in patients who have taken antihypertensive two drug combination therapy

7. DISCUSSION

The various classes of antihypertensive drugs have different effects on blood glucose metabolism. Various studies have demonstrated that some antihypertensive therapies can promote the development of type 2 diabetes mellitus. Combination therapy has been recommended as a potential first line therapy in clinical practice, especially for higher-risk patients, such as those with stage 2 hypertension. The present studies compare the glycemic level of diabetic hypertensive patients who are on antihypertensive combination therapy.

Out of 200 cases with both diabetes mellitus and hypertension, 48 patients were between the age group of 40-50 years among which 32 patients were male and 16 were female, 64 patients were between 51-60 years among which 40 patients were male and 24 were female, and 88 patients were between 61-70 years of age among which 56 patients were male and 32 were female. (Table 1)

In this study, there was male preponderance in patients having both hypertension and diabetes of the age group 61-70 was seen, this was similar to the studies conducted in India (Yasmeen *et al.*, and Jaganan *et al.*,) USA (Everett *et al.*,) Nepal (Pandaya *et al.*,) and Australia (White *et al.*,) which reported that the incidence of hypertension with diabetes mellitus was higher in males compared to females [5-9].

This could probably be due to significantly higher awareness, treatment, and control rates among women than men as supported by a data from the 2007 to 2010 National Health and Nutrition Examination Survey [10].

The coexistence of hypertension and diabetes mellitus is more dangerous and it considerably increases the macrovascular complications, including CVA, CHD, congestive heart failure and peripheral vascular disease, and is responsible for excessive cardiovascular mortality [11]. Our findings showed that 56 out of 128 male patients and 20 out of 72 female patients had CVD and was markedly increased in men (43.75%) with diabetes than in women

(27.77%). (Table 2) But this different from the study conducted by Li-Nien *et al.*, where the prevalence of CVD was more in women with diabetes and hypertension [12]. In this study, CVA's were commonly found in male (33.59%) than in female (38.88%) and renal failure patients were more among male patients (22.65%) than in female (33.33%).

Combination therapy has been recommended as a potential first line therapy in clinical practice, especially for higher-risk patients, such as those with stage 2 hypertension. In this study out of 200 cases collected 56 (28%) patients were on antihypertensive mono therapy and 112 (56%) patients were on antihypertensive combination therapy and the rest of the patients didn't knew the medicines that they were taking. (Table 4)

Here the most commonly used antihypertensive 2 drug combination therapy used was CCB and BB (31.25%) followed by diuretics and BB (29.46%). This is in agreement with the study conducted by Panda *et al.*, and Paulose *et al.*, wherein the most common 2-drug combination prescribed was CCB (30.3%) and BB (18%) [13,14].

But this was different from the study conducted by K.Kousalya *et al.*, where the most commonly used antihypertensive 2-drug combination was ACEI and CCB [15].

In contrast to this, our study shows CCB in combination with BB as the most commonly prescribed drug therapy for treating hypertension in patients with diabetics. (Table 5)

Here, out of 112 patients 35 patients had an elevated RBS reading (above 300 mg/dl). In this 34 patients, 20 patients (58.82%) were on diuretics (furosemide) and BB (atenolol) combination therapy. 2 patients (5.88%) were on CCB (amlodipine) and BB (atenolol) combination therapy, 8 patients (23.53%) were on ACE (enalapril) and BB (atenolol), 4 patients (11.76%) were on diuretics (furosemide) and ACE (enalapril) combination therapy and No patient on ACE (enalapril) and CCB (amlodipine) combination therapy had elevated RBS glucose level. FBS level was elevated (above 200mg/dl) in 45 patients. Wherein, 26 patients (57.78 %) were on diuretics (furosemide) and BB (atenolol) combination therapy. Table 5 and 6 shows that the patients under diuretic (furosemide) therapy in combination with beta blocker (atenolol) had an elevated blood glucose level in comparison with the patients under other antihypertensive combination therapy. This was in agreement with the study conducted by Bakris GL *et al.*, wherein the non-vasodilating beta-blockers such as atenolol and metoprolol have been reported to worsen insulin sensitivity [16]. But a study conducted by Bryan Wai *et al.*, showed that selective BBs do not worsen glycemic control in subjects with hypertension and type 2 diabetes mellitus [17]. In the FACET, amlodipine decreased fasting serum glucose in patients with type 2 diabetes mellitus and hypertension [18].

8. LIMITATIONS

The duration of this study was short to take the follow up of the cases and to monitor the patient. Major drawback of the study was the limited number of cases and an uneven number of cases in various combination therapies.

9. CONCLUSION

In the present study the most commonly used antihypertensive 2 drug combination therapy used was CCBs and BBs (31.25%) followed by diuretics and BBs (29.46%). But the glycemic control in patients who were on by diuretics and BBs was not satisfactory. Patients who were on diuretics and BBs combination therapy showed elevated blood glucose level in comparison with patients who were on other antihypertensive combination therapy. This shows that combination of BBs and diuretics cannot be safe in diabetic hypertensive patients. However the efficacy this drug combination requires further scrutiny.

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Authors Contributions

The first author (chandhni ES) carried out the complete experimental work, the corresponding author (sujitha PJ) guided the project, sambathkumar R contributed in the approval.

Conflict of Interest

The authors declare that there is no conflict of interest.

PATIENT INFORMATION FORM

Dear participant,

We are students of JKK.NATTRAJA COLLEGE OF PHARMACY currently conducting a project entitled “ Comparison of antihypertensive combination therapy and glycemic control in diabetic hypertensive patients ”. As a part of project, we need to collect data including past, social and family history, history of drug, lab reports and current medical data. However, no identifiable personal data will be disclosed.

Thank you very much for your kind participation.

CONSENT FORM

I, _____ have read and understood the above information. I hereby allowing my data for the accomplishment of their thesis.

Signature of participant

Date

Translated by:

REFERENCES

- Dobesh PP. Managing Hypertension in Patients with Type 2 Diabetes Mellitus. *Am J Health Syst Pharm*. 2006;63(12):1140-49.
- Vikas Jhawar, Sumeeth Guptha, Bimal KA, Partha Roy, Vipin Saini. Prevalence and risk factors of essential hypertension and new onset of diabetes in essential hypertension in rural population of Haryana. *Int J Pharm Pharm Sci*. 2018;10(2):142-48.
- Barrett C, Criqui MH, Klauber, Holdbroo M. Diabetes and hypertension in a community of older adults. *Am J Epidemiol*. 1981;113(15):269-276.
- Drury PL. Diabetes and arterial hypertension. *Diabetologia*. 1983;24(1):88-91.
- Yasmeen N, Varma RK, Siddiqua SS, Donepudi A. Efficacy and tolerability of different antihypertensive drugs in patients with mild to moderate hypertension in a tertiary care hospital prospective, comparative study. *Arch Appl Sci Res*. 2011;3(2):436-43.
- Janagan T, Kavitha R, Sridevi SA, Veerendra V. Prescription pattern of antihypertensive drugs used in hypertensive patients with associated type 2 diabetes mellitus in a tertiary care hospital. *Int J Pharm Rev and Res*. 2014;3(1):1-5.
- Everett BM, Glynn RJ, Danielson E, Ridker PM. Combination therapy versus monotherapy as initial treatment for stage 2 hypertension: A prespecified subgroup analysis of a community-based, randomized, open-label trial. *Clin Ther*. 2008;30(4):661-72.
- Pandaya S, Reyad M, Panthi VK, Pandey M, Maharjan L. Effectiveness of antihypertensive agents among hypertensive patients of Nepal. *Int Res J Pharm*. 2014;5(2):903-09.
- White F, Wang L, Jelinek HF. Management of hypertension in patients with diabetes mellitus. *Exp Clin Cardiol*. 2010;15(1):5-8.
- Curtin LR, mohadjer L K, Dohrmann SM, et al. national health and nutrition examination survey: sample design, 2007-2010. *vital health statistics* 2.2012;(155):1-39.
- D Giri Rajasekhar, Guru prasanna D, Chandrakanth P. Prescribing pattern of antihypertensive drugs based on compelling indications with hypertension. *Int J Pharm Pharm Sci*. 2016;(2)6:72-75.
- Li-Nien Tseng, Yao-Hsien Tseng, Yi-Der Jiang, et al. Prevalence of hypertension and dyslipidemia and their associations with micro- and macrovascular diseases in patients with diabetes in Taiwan: An analysis of nationwide data for 2000-2009. *J Formos Med Assoc*. (2012);111(3):625-36.
- Panda BB, Pati MR, Sahu PK. Survey of prescription pattern of antihypertensive drugs in hypertensive and diabetic hypertensive patients. *Asian J Pharm Clin Res*. 2015;8(1):250-52.
- Paulose RM, LaxminarayanaBairy k, prabhu MM, Eesha BR, VeenaNaak, AmrutaTripathy. Comparison of efficacy and adverse drug reactions of monotherapy versus combination therapy of antihypertensives among diabetic hypertensive patients in a tertiary care hospital. *Asian J Pharm Clin Res*. 2017;10(2):385-391.
- Kousalya K, Sowmya C, Manjunath S, Ramalakshmi R, Saranya P, Chamundeeswari D. Prescribing trend of antihypertensive drugs in hypertensive and diabetic hypertensive patients. *Asian J Pharm Clin Res*. 2012;5(4):116-18.
- Bakris GL, Fonseca V, Katholi RE, et al. Metabolic effects of carvedilol vs metoprolol in patients with type 2 diabetes mellitus and hypertension: A randomized controlled trial. *J Am Med Assoc*. 2004;292(3):2227-236.
- Bryan WaiI, Leighton GK, David LH, Michelle O, Louise MB, Piyush M. Beta blocker use in subjects with type 2 diabetes mellitus and systolic heart failure does not worsen glycaemic control. *Cardiovascular Diabetology*. 2012;11(1):14.
- Tatti P, Pahor M, Byington RP, et al. Outcome results of the Fosinopril Versus Amlodipine Cardiovascular Events Randomized Trial (FA CET) in patients with hypertension and NIDDM. *Diabetes Care*. 1998;21(4):597-603.