

Antihypertensive agents in systemic hypertension associated with Type 2 diabetes in a tertiary care hospital

Tanaji R. Shende*, Riyaz A. Siddiqui, Harshal M. Mahajan

Department of Pharmacology,
NKP Salve Institute of
Medical Sciences and
Research Centre, Nagpur,
Maharashtra, India

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***Correspondence to:**

Dr. Tanaji R. Shende,
Email: tanaji.shende@
rediffmail.com

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ABSTRACT

Background: Hypertension and diabetes mellitus are both chronic disorders and when they occur as co-morbidities create havoc by presenting with a plethora of morbidity and mortality. Both require drug treatment over a long period of time, which calls for stringent analysis of prescribing trends of the same.

Objectives: The present study was intended to analyze prescribing pattern and establish prescribing trends of anti-hypertensive drugs (AHD) in hypertensive diabetic patients.

Methods: The present study was a record based, randomized, non-interventional study of 2 years duration conducted at a tertiary care hospital of central India. Prescriptions from 400 case records of hypertensive diabetics were obtained from the medical record section. Demographic details, blood pressure, and AHDs prescribed were systematically entered in pre-validated case record form. All data were thoroughly analyzed for fallacies and appropriateness.

Results: Among 400 patients, 221 were males, and 179 were females. Monotherapy was used in 366 (91.5%) patients while combination therapy was used in 34 (8.5%) patients. Most commonly used combination was angiotensin converting enzyme inhibitor (ACEI)+calcium channel blocker (CCB), while in monotherapy CCB>ACEI>beta blocker>diuretic>angiotensin II receptor blocker were most commonly prescribed.

Conclusion: The present study represents trend and attitude of physicians in prescribing AHDs. On comparing with Joint National Committee 7 guidelines, the majority of the cases deviated from the guidelines, mostly in a choice of AHDs and Fixed dose combination.

Keywords: Hypertension, Antihypertensive agents, Diabetes, Joint National Committee 7

INTRODUCTION

Hypertension (HTN) is now considered as potent revampable planetary risk factor keeping in mind, the reduction in morbidity and mortality of cardiovascular origin.^{1,2} From various studies conducted globally etiological link have been established between HTN and various hemorrhagic and ischemic events such as stroke, coronary artery disease, congestive heart failure, and last but not the least deteriorating renal status;^{3,4} and majority of morbidity and mortality in such events have been attributed to erroneous treatments.⁵ However, this is only half of the picture, the other part being portrayed by diabetes mellitus (DM) associated with HTN. The findings of lofty occurrence of Type 2 DM in hypertensive patients coupled with increased incidence of HTN in diabetics as compared to non-diabetics is the main concern of the hour.⁶ This finding is eye catching

not plainly because of their strength of association, but from the fact that they work so much harmoniously that morbidity and mortality are increased multiple folds as compared to that in isolated disease⁷ due to soaring occurrence of macrovascular and microvascular complications.⁸ In India, HTN acquires even more staid status, as an indicated by 10% of all deaths attributable to the disease⁹ and noticeably higher incidence in the urban population when compared to rural.¹⁰ It is a well-known fact that HTN being a chronic disease, require life-long treatment and pharmacotherapy for the same, effectively controls blood pressure, when given appropriately.¹¹ Rational use of a drug is the essence for the successful treatment of any disease.¹² To help the physicians with same intention, guidelines are published for various diseases by concerned authorities, in this case, the Joint National Committee 7 guidelines have been established for appropriate use of anti-hypertensive drugs

(AHDs).¹³ However, on reality check, these guidelines are casually bypassed by the physicians as indicated by various studies.¹⁴⁻¹⁸ On a broader perspective, not only the prescribers, but also the pharmacists, drug companies, and health authorities are collectively responsible for this irrational prescribing.¹⁹ Therefore, it is need of the hour to carry out such drug utilization studies from time to time, so that all persons involved in irrational prescribing circuit are familiarized with their fallacies and its impact on health care, so that can rectify them and thus help in reducing the cost and adverse effects due to such irregularities and increasing the efficacy of treatment of the disease.

Aims and objectives

The intention of the present study was to analyze the pattern of drug utilization of AHDs in indoor patients, identify fallacies and to scrutinize for adherence to Joint National Committee 7 (JNC 7) guidelines.

METHODS

The present study was a randomized, retrospective, non-interventional record based study conducted at NKP Salve Institute of Medical Sciences and Research Centre and Lata Mangeshkar Hospital, Nagpur. The study was initiated after obtaining ethics clearance from Institutional Ethics Committee. The study duration was of 2 years.

Inclusion criteria

1. Patients with age >18 years, irrespective of sex
2. Patients with a diagnosis of HTN with DM.

Exclusion criteria

1. Eclampsia and pre-eclampsia
2. Age <18 years
3. Patients with recent surgery, especially on the pancreas.

After stringent search from about 700 case records obtained from medical record section and filtering them through inclusion and exclusion criteria, finally 400 case records were included in the study. Furthermore, a continuous review of literature related our study was done on daily basis to stay updated and to compare and contrast the findings. All the demographic details like blood pressure, AHDs either monotherapy or fixed dose combination were recorded systematically and analyzed under following heads as per World Health Organization (WHO) prescribing indicators 2003:²⁰

1. Average number of drugs per prescription
2. Percentage of drugs prescribed by generic name
3. Percentage of prescribed drugs given as injectables
4. Percentage of drugs prescribed from essential drug list (WHO and Indian).^{21,22}

Furthermore, included were

5. Demographic details like age, men: women ratio
6. Percentage of prescriptions as monotherapy and combination therapy.

The data were analyzed in Microsoft Excel 2013.

RESULTS

Of total 400 records of hypertensive diabetics, 221 were males, and 179 were females. Totally, 376 patients were diagnosed with Type 2 DM, out of which 214 were males and 162 were females, and 24 patients were diagnosed with Type 1 DM (7 males and 17 females). Age-wise, maximum patients were in the age group >60 years followed by 45-60 years and least in 18-45 years (Figure 1). The average number of drug/prescription was 2.6. No drug was prescribed as generic, while 8% of total prescribed drugs were given in injectable form, 16% of drugs were found in WHO essential medicine list and 52.6% from Indian list (Table 1). Monotherapy was used in 91.5%. Sex-wise AHDs prescribed is demonstrated in Figure 2. Among monotherapy, drugs from angiotensin converting enzyme inhibitor (ACEI) and calcium channel blocker (CCB) class were most commonly

Table 1: Prescribing indicators.

Parameter	Number (%)
Average number of drugs per prescription	2.6
Number of injectables	32 (8)
Number of FDCs prescribed	34 (8.5)
Number of drugs prescribed from WHO-EML	3 (16)
Number of drugs prescribed from EML-India	10 (52.6)
Number of drugs prescribed by generic names	0

FDC: Fixed dose combination, WHO-EML: World Health Organization-Essential medicine list

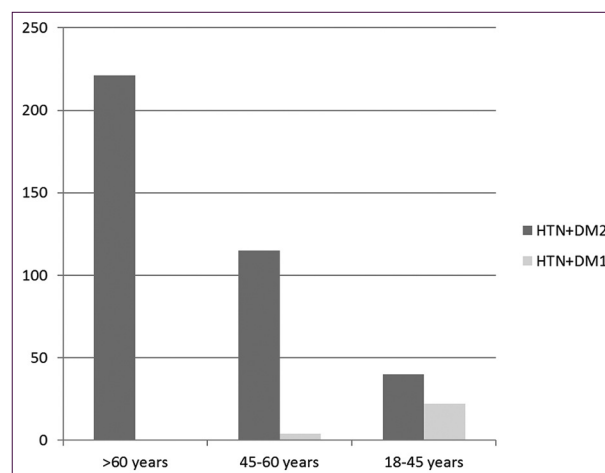


Figure 1: Age-wise patient distribution.

prescribed in both sexes, while least used was clonidine in males and prazosin in females. Combination therapy was used in 8.5% patients among, which ACEI+CCB and ACEI+diuretics were used most commonly and least commonly used respectively, in either of the sexes (Table 2). Among the classes, Ramipril was most commonly used in ACEI, losartan in angiotensin II receptor blocker (ARB), Amlodipine in CCB, Atenolol in beta blockers, thiazides in diuretics (Table 3).

DISCUSSION

In the present study, among the monotherapy both CCB and ACEI were prescribed in the majority, with almost equal frequency, which is in contrast with findings of other studies.²³ Among the combination therapy, most commonly used combination was ACEI+CCB, which is dissimilar from findings of other such studies.²⁴⁻²⁶ However, these findings were corroborated in some studies.²⁷ The most preferred route was oral (Figure 3). The average number of drugs per prescription was 2.6 which was found to be around 5 in one study.²⁸ ACEI therapy should be included as a mandatory component in all regimens of HTN+DM as per JNC 7 guidelines, since they inhibit the breakdown of bradykinin, which is vasodilator, and also it increases glucose entry into

the skeletal muscles by increasing the translocation of GLUT 4 receptors to the cell membrane.²⁹ Furthermore, it is now a well-known fact from the findings of various studies that considerable number of hypertensive diabetics advance to nephropathy.³⁰ ACEIs have a favorable and rescue role in diabetic nephropathy through following mechanisms:

- a. It reduces albuminuria
- b. Reduces glomerular capillary pressure, by relieving vasoconstriction on efferent arteriole, by limiting the formation of angiotensin II

Table 2: Fixed dose combinations prescribed.

FDCs	Frequency of use
ACEI+beta blocker	8
ACEI+CCB	12
ACEI+diuretic	0
ARB+beta blocker	5
CCB+beta blocker	4
CCB+diuretic	3
ARB+betablocker+CCB+Diuretic	2

FDCs: Fixed dose combination, ACEI: Angiotensin converting enzyme inhibitors, ARBs: Angiotensin II receptor blocker, CCB: Calcium channel blockers

Table 3: Sex-wise frequency of individual AHDs prescribed.

AHDs	Drug	Frequency of use (n=366)	
		Male (n=204)	Females (n=162)
ACEI	Ramipril	41	31
	Enalapril	14	16
	Lisinopril	6	3
ARBs	Losartan	7	8
	Telmisartan	2	2
	Olmesartan	3	1
Beta blockers	Atenolol	23	19
	Metoprolol	9	3
	Nebivolol	1	4
	Carvedilol	1	0
CCB	Amlodipine	42	36
	Diltiazem	14	9
	Nifedipine	11	6
Diuretics	Verapamil	2	0
	Frusemide	7	6
	Thiazides	13	12
Alpha blockers	Spironolactone	1	1
	Prazosin	5	1
Central sympatholytics	Clonidine	2	4

AHDs: Anti-hypertensive drugs, ACEI: Angiotensin converting enzyme inhibitors, ARBs: Angiotensin II receptor blocker, CCB: Calcium channel blockers

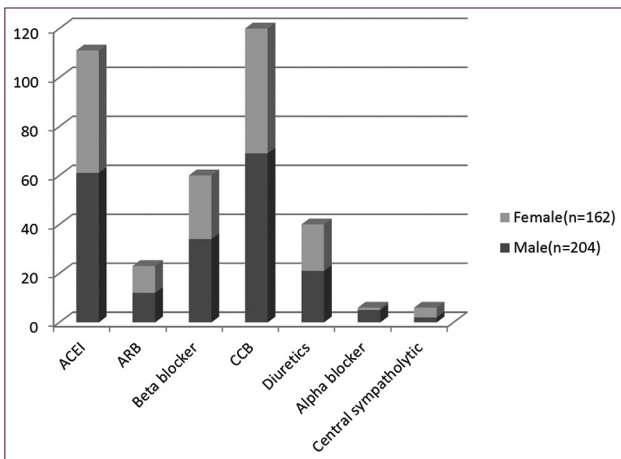


Figure 2: Sex-wise distribution of anti-hypertensive drugs prescribed in the study group.

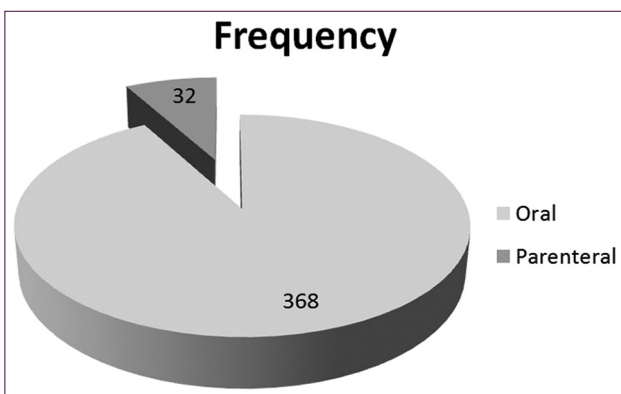


Figure 3: Route of administration.

- c. Promote renal blood flow through dilation of renal vasculature
- d. Inhibit glomerular hypertrophy and excess of mesangial matrix accumulation, induced by angiotensin II.³¹

It is painstaking to notify that despite these known facts and established JNC 7 guidelines, ACEIs and ARBs were not prescribed even in half of the patients in the present study as was found in other studies also,^{7,24,32-34} thus indicating a large scale problem. In the present study, CCBs were most commonly prescribed, and this may be justified by the fact that CCBs effectively decrease BP to target level with additional renoprotective action. Moreover, the dose of amlodipine need not be reduced in renal insufficiency.³⁵

CONCLUSION

JNC 7 guidelines have been ornately recognized for effective diagnosis and apposite treatment of HTN and associated co-morbidities. It clearly states the mandatory role of ACEIs/ARBs in all AHD regimens in the treatment of hypertensive diabetics, and this was reflected in the present study to some extent. However, this beneficial use of ACEI/ARB in combination with CCB should be used in all possible cases, to save lives and cost, before it is too late since “a stitch in time saves nine.”

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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