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PRESCRIBING PATTERN OF ANTIHYPERTENSIVES IN INDIVIDUALS WITH HYPERTENSION ALONE AND WITH COEXISTING DIABETES MELLITUS – A COMPARATIVE STUDY

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ABSTRACT

Objective: Analysis of prescribing pattern of antihypertensives in patients with hypertension alone and with coexisting diabetes mellitus.

Materials and Methods: A cross sectional study was conducted in an outpatient and inpatient department of general medicine at JJM Medical College hospital for a period of 3 months (July 2011 to September 2011). Prescriptions of the patients were collected and relevant data was entered in the preformed proforma and analyzed.

Results: A total of 210 prescriptions were analyzed using chi square test. Out of which 126 prescriptions were of patients with hypertension alone which contain calcium channel blockers (30%), beta blockers (26%), angiotensin receptor blockers (15%), angiotensin converting enzyme inhibitors (4%) and fixed dose combinations of angiotensin receptor blockers with hydrochlorothiazide (11%) and combination of amlodipine with hydro-chlorothiazide (2.5%).84 Prescriptions of hypertension with coexisting diabetes mellitus had calcium channel blockers (24%), angiotensin converting enzyme inhibitors (19%), angiotensin receptor blockers (13%), beta blockers (13%), and fixed dose combinations of angiotensin receptor blockers with hydrochlorothiazide (18%) and combination of amlodipine with hydrochlorothiazide (6%).[χ^2=17.01, p=o.oo4]

Conclusion- The present study shows that angiotensin converting enzyme inhibitors because of its beneficial effects which are well known are more commonly prescribed drugs in individuals with hypertension with coexisting diabetes mellitus. Calcium channel blockers and newly introduced angiotensin receptor blockers alone or in combination with hydrochlorothiazide are preferred drugs in both the study groups. Beta blockers are less preferred in patients of hypertension with coexisting diabetes mellitus for obvious reasons.

INTRODUCTION: Hypertension is highly prevalent risk factor for not only for cardiovascular morbidity and mortality but also for other end organ damage. Holistic approach in treatment of hypertension is by antihypertensive drugs. Availability of numerous antihypertensives gives physicians several options to individualize the therapy [1-5]. Due to this fact there will be change in the prescribing pattern from patient to patient and physician to physician.

The reason for this variation in the prescribing pattern is due to the conflict of interest of physician, some doctors are early adapters of new interventions but others are more conservative [6].

Based on the evidence, guidelines are revised regularly and newer interventions are advised. Previously a single drug therapy was started and titrated to produce a required effect and stopped when the dose required is more than maximum tolerated dose a second drug is added to the therapy. But recent guidelines is to start with two drugs be it free drug combination or fixed dose combination which are acting at different target sites. There are studies showing that fixed dose combination is superior to free drug combination in terms of compliance [7, 8].

Thousands of FDCs are dumped into market but only few get FDA approval. FDA approved FDCs are not expected to interact adversely with each other but may show interactions when prescribed with other drugs. Disadvantages of FDCs: they add to the financial burden and cannot be titrated depending on the individual requirements [9].

Other factors that has an effect on the prescribing pattern are aging, pregnancy and co morbid conditions, such as diabetes mellitus, dyslipidemia etc. Hypertension and diabetes are the chronic medical conditions that coexist. There may be casual relationship between hypertension and diabetes. Medical survey done in US reveals that there are three million population who have hypertension co existing with diabetes. Obesity may be a precipitating factor for hypertension and non-insulin dependent diabetes mellitus.

Individuals with insulin dependent diabetes mellitus generally become hypertensive only with the onset of nephropathy. Glucose intolerance, insulin resistance and hyperinsulinemia frequently occur with essential hypertension. Therefore, JNC7 Guidelines mentions diabetes mellitus as compelling indication to treat individuals with prehypertension by drug therapy. The recommended strategy is to lower BP below 130/85 mm Hg [10-13].

Objective: Analysis of prescribing pattern of antihypertensives in patients with hypertension alone and with coexisting diabetes mellitus.

Study Design: A cross sectional study was conducted in an Out Patient and In Patient Department of General Medicine at JJM Medical College Hospital, Davangere. Data was collected for duration of 3 months (July 2011 to September 2011). Study was carried out after obtaining the permission from institutional ethical committee. Permission was also obtained from Head of Department General Medicine to access records. Prescriptions of the patients were collected and relevant information was entered in the preformed proforma and analyzed

Study Setting: Inpatient and Outpatient Department of General Medicine attached to JJM Medical college Hospital, Davangere.

Sample Size: During the period of 3 months (July-September 2011) a total of 210 prescriptions of patients diagnosed to have hypertension with or without coexisting diabetes mellitus were collected.

Informed Consent: Not applicable as the study involved only retrospective analysis of records.

Statistical Analysis: In this study, Data will be analyzed using Descriptive Statistics. Analysis of pattern of prescription between the groups i.e. hypertension without diabetes and with diabetes is done using chi square test.

RESULTS: This cross sectional study involved 210 prescriptions of patients treated in outpatient and inpatient department. Patient were divided into 6 groups depending on the ages, i.e., 35- 44, 45- 54, 55-64, 65- 74, 75- 84 & ≥ 85 years.

Demographic Profile of the Study Population: The Demographic characteristics of the patients are as shown in the **Table 1**. Among 210 prescriptions number of Male is 110, number of Female is 100 suffering from hypertension with or without coexisting diabetes mellitus.

Among all the prescriptions 72 patients belong to 65-74 years of age, 44 patients belong to 55-64 years and 42 patients belong to 45-54 years of age. Total of 105 patients constitute geriatric population that is age ≥ 65 years.

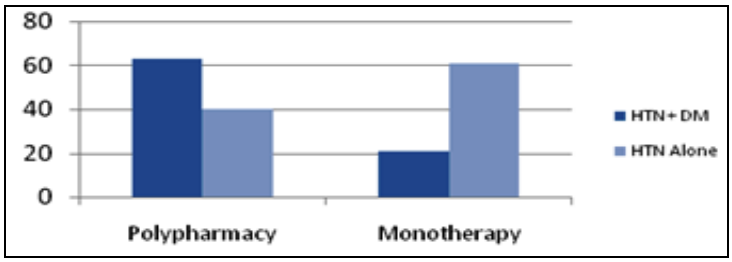
TABLE 1: DEMOGRAPHIC DISTRIBUTION OF ANTIHYPERTENSIVE PATIENTS

Age [Years]	Male	Female	Total No. of Patients
35-44	12	7	19
45-54	23	19	42
55-64	25	19	44
65-74	39	33	72
75-84	8	19	27
≥85	3	3	6

In **Table 2**, number of patients receiving monotherapy and polypharmacy in hypertension with or without coexisting diabetes mellitus is tabulated. Among 210 prescriptions, 126 were of hypertensives without diabetes in which 86 patients received monotherapy. Out of 84 patients diagnosed hypertensives with coexisting diabetes mellitus, majority i.e., 63 patients received polypharmacy.

TABLE 2: MONOTHERAPY VERSUS POLYPHARMACY

	Hypertension + Diabetes Mellitus	Hypertension Alone
Polypharmacy	63	40
Monotherapy	21	86
Total	84	126

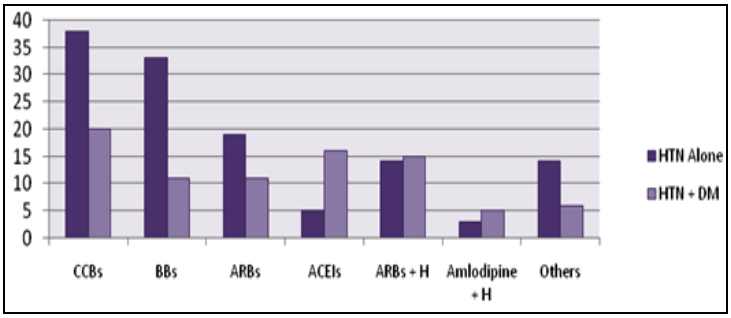


GRAPH 1: DEPICTING MONOTHERAPY VERSUS POLYPHARMACY

In this study, the main focus is on variation of prescribing pattern between hypertensives alone and hypertensives with coexisting diabetes mellitus. So acquired data is further sub classified into hypertensives alone and hypertensives with coexisting diabetes mellitus and categorized according to different age groups.

TABLE 3: FREQUENCY OF INDIVIDUAL GROUPS OF ANTI-HYPERTENSIVES PRESCRIBED IN HYPERTENSIVES ALONE AND HYPERTENSIVES WITH COEXISTING DIABETES MELLITUS

Drugs	HTN ALONE		HTN+DM	
	Number	Percentage	Number	Percentage
CCBs	38	30	20	24
BBs	33	26	11	13
ARBs	19	15	11	13
ACEIs	5	4	16	19
ARBs+H	14	11	15	18
Amlodipine + H	3	2.5	5	6
Others	14	11.5	6	7
Total	126	100	84	100



GRAPH 2: REPRESENTS COMPARISON OF FREQUENCY OF DIFFERENT GROUPS OF ANTIHYPERTENSIVE DRUGS PRESCRIBED IN HYPERTENSIVES ALONE AND IN HYPERTENSIVES WITH COEXISTING DIABETES MELLITUS.

[CCBs - Calcium Channel Blockers, BBs - Beta Blockers, ARBs - Angiotensin Receptor Blockers, ACEIs - Angiotensin Converting Enzyme Inhibitors, ARBs+H - Fixed dose combination of Angiotensin Receptor Blockers and Hydrochlorothiazide , Amlodipine + H - Fixed dose combination of Amlodipine and Hydrochlorothiazide]

Various groups of antihypertensives were prescribed to the participants of the study. A total of 210 prescriptions were analyzed using chi square test. Out of which 126 prescriptions were of patients with hypertension alone which contain calcium channel blockers (30%), beta blockers (26%), angiotensin receptor blockers (15%), angiotensin converting enzyme inhibitors (4%) and fixed dose combinations of angiotensin receptor blockers with hydrochlorothiazide (11%) and combination of amlodipine with hydrochlorothiazide (2.5%).

84 Prescriptions of hypertension with coexisting diabetes mellitus had calcium channel blockers (24%), angiotensin converting enzyme inhibitors (19%), angiotensin receptor blockers (13%), beta blockers (13%), and fixed dose combinations of angiotensin receptor blockers with hydrochlorothiazide (18%) and combination of amlodipine with hydrochlorothiazide (6%). So, most frequently prescribed antihypertensive drugs in both the groups were calcium channel blockers. Other antihypertensives prescribed include Clonidine and different FDCs such as Olmesartan + Amlodipine, Ramipril + Hydrochlorothiazide, Telmisartan + Amlodipine, Amlodipine + Atenolol, Losartan + Hydrochlorothiazide etc., [χ^2 = 17.01, p = 0.004]

DISCUSSION: The field of medicine has evolved from art form through experienced based medicine to evidence based medicine, from palliation therapy to preventive therapy.

Prescription based survey is one of the methods to produce evidence required to improvise the standards of clinical practice. A continuous supervision is therefore necessary through such kinds of systematic audit, which provide feedback from the physician and help to promote rational use of drugs.

In general, prevalence of hypertension increases as the age advances [4]. In the present study, it is observed that 25% of patients were less than 50 years of age and 75% of patients were more than 50 years of age.

Now the latest recommendations are to start the combination of two fixed or free drugs.[12] In our observational study 75% of patients with coexisting diabetes were prescribed polypharmacy and for rest monotherapy would suffice. But we do not know how many were started with polypharmacy. One more reason for polypharmacy is, sometimes blood pressure cannot be controlled by a single drug even after increasing the dose to maximum tolerable dose further increase will lead to adverse effects then second drug is added to the therapy.

Recommendations for treatment of elevated blood pressure according to JNC7 guidelines depend on staging of hypertension and whether they are associated with or without compelling indications. Some of the compelling indications mentioned in JNC 7 are heart failure, post myocardial infarction, diabetes mellitus, and chronic kidney disease. Prehypertension without compelling indications are advised life style modifications and pharmacotherapy is required if associated with compelling indications.

Here, target is to achieve BP less than 130/85 mm Hg. In Stage I, recommendation is to start with thiazide diuretics, combination of thiazide and other drugs such as CCBs, ACEIs, ARBs and BBs can be considered. In Stage II, two drug combinations are to be advised to most of the hypertensives. In both Stage I and II with compelling indications combination therapy is recommended [12].

In our study most frequently prescribed drug in hypertensives without diabetes is CCBs (30%), followed by BBs (26%) and ARBs (15%). The Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial compared the metabolically neutral calcium channel blockers to an ACE inhibitor and reported a 17% reduction in the incidence of diabetes in the ACE inhibitor group. But here ACE inhibitors as monotherapy and combination therapy of ACE inhibitors and Hydrochlorothiazide amounts to approximately 8%. Thiazides are mostly prescribed in combination with other groups of antihypertensives makes up to 20% of prescriptions [14, 15].

In Hypertensives with coexisting Diabetes Mellitus CCBs (24%) are again most frequently prescribed drugs followed by ACE inhibitors (19%), ARBs (13%). Important observation to be made here is FDCs of ARBs and Hydrochlorothiazide amounts to 18% of prescriptions.

ARBs alone or in combination with Hydrochlorothiazide make considerable amount of prescriptions in this study. JNC 7 guidelines mention that ACE Inhibitors and ARBs based treatment favorably affect the progression of diabetic nephropathy and reduce albuminuria and ARBs have been shown to reduce progression to macroalbuminuria [12, 16, 17].

CONCLUSION: The present study shows that Angiotensin converting enzyme inhibitors because of its beneficial effects which are well known are more commonly prescribed drugs in individuals with hypertension with coexisting diabetes mellitus. Calcium channel blockers because they are metabolically inert are frequently prescribed group of antihypertensives in both the study groups. Angiotensin receptor blockers alone or in combination with hydrochlorothiazide are preferred drugs especially in hypertensives with coexisting diabetes mellitus as they favorably affect the disease progression of diabetic nephropathy. Beta blockers are less preferred in patients of hypertension with coexisting diabetes mellitus for obvious reasons.

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