Management Of Hypertension With Concomitant Coronary Artery Disease: Results From The Imperial Study-4

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Citation

S Kalra, N Agrawal, F Hussain, S Mitra. *Management Of Hypertension With Concomitant Coronary Artery Disease: Results From The Imperial Study-4* . The Internet Journal of Family Practice. 2009 Volume 8 Number 2.

Abstract

THE IMPERIAL (Indian Medical Practitioners Expressions Regarding Drug Intervention In All Aspects of MetaboLic Syndrome) study, which assessed Indian physicians' prescribing habits related to metabolic syndrome, also assessed their preferred management strategies in hypertension associated with coronary artery disease (CAD). This paper reviews the results related tocoronary artery disease, obtained from the IMPERIAL study. There is a clear consensus for the use of both beta-blockers and angiotensin converting enzyme inhibitors as first line antihypertensive therapy in patients after myocardial infarction, and for beta-blockers in patients with angina.It is hoped that these results stimulate discussion and debate, on the management of hypertension in coronary artery disease, while encouraging doctors to follow existing rational guidelines.

INTRODUCTION

Though hypertension is a common co-morbid condition associated with angina or myocardial infarction, and multiple recommendations/ consensus guidelines are available to guide antihypertensive therapy in patients with diabetes, no large study is available to assess prescribing habits of Indian physicians in this subset of patients.

Minimal work has been done to explore the relative popularity of various classes of anti-hypertensive drugs in patients with hypertension and coronary artery disease treated by consultant physicians in India.

THE IMPERIAL (Indian Medical Practitioners Expressions Regarding Drug Intervention In All Aspects of MetaboLic Syndrome) study, which assessed Indian physicians' prescribing habits related to metabolic syndrome, also assessed their preferred management strategies in hypertension associated with angina and myocardial infarction.

This paper reviews the results related to coronary artery disease, obtained from the IMPERIAL study. It is hoped that these results form the basis for an exchange of ideas, and discussion on the topic, and finally lead to a consensus on the management of hypertension associated with heart disease.

MATERIAL & METHODS

The objective of this nationwide survey of physicians, diabetologists and cardiologists across India, performed in 2009, was to assess their practicing habits and attitudes related to hypertension and other aspects of metabolic syndrome.

A structured questionnaire was distributed to 482 doctors attending continuing medical education programmes. These included 59 (12.24%) from North zone, 131 (27.18%) from East zone, 80 (16.6%) from West, 92 (19.09%) from Central zone and 120 (24.93%) from South zone.

The cohort included 472 men and 10 ladies, all with a minimum qualification of MD Medicine, with an average age of 45.55 ± 5.0 years and average experience of 20.25 ± 5.0 years.

Data related to coronary artery disease is available for 307 doctors. These included 58 (18.89%) from North zone, 77 (25.08%) from East zone, 80 (26.05%) from West and 92 (29.96%) from Central zone

RESULTS

First line anti hypertensive monotherapy preferred by doctors in general patients was a beta-blocker by 62.03%, a calcium channel blocker by 52.90%, and a diuretic by 44.40 % physicians. Angiotensin receptor blockers (ARBs) and angiotensin converting enzyme (ACE) inhibitors were used

less often, by just 34.85% and 28.01% doctors respectively. (Table 1)

Figure 1

Table 1: Choice of Antihypertensive drugs in Hypertension with or without diabetes(n=482)

Choice of Monotherapy	Hypertension without Diabetes	Hypertension with Diabetes
ACE-Inhibitor	135(28.01%)	379(81.76%)
ARBs	168(34.85%)	349(72.41%)
Beta-blocker	299(62.03%)	51(10.58%)
Calcium channel blocker	255(52.90%)	98(20.33%)
Diuretics	214(44.40%)	66(13.69%)

Figure 2

Table2: Choice of Anti hypertensive Drugs in Hypertensive Patients with myocardial infarction/angina (n=307)

Choice of Drug	Myocardial infarction	Angina pectoris
ACE-Inhibitor	200 (65%)	76 (25%)
ARBs	68 (22%)	45 (15%)
Beta-blocker	200 (65%)	257 (84%)
Calcium channel blocker	35 (11%)	90 (29%)
Diuretics	44 (14%)	22 (7%)

In patients with angina, there was a clear consensus as to the preferred antihypertensive, with 84 % doctors preferring beta-blockers, and only 29% choosing calcium channel blockers. Only 15% doctors wrote angiotensin receptor blockers, 25% gave ACE inhibitors and 7% preferred diuretics. (Table 2)

In patients with myocardial infarction, there was a similarly clear consensus as to the preferred antihypertensive, with 65% doctors preferring ACE inhibitors, and 65% choosing beta blockers. Only 22% doctors wrote ARBs, 11 % gave calcium channel blockers and 14% preferred diuretics.(Table 2)

Thus, patients with angina were more likely to be prescribed the commonly used classes of beta-blockers, but less likely to be given calcium-channel blockers. No clear-cut reasons were elicited regarding this individual preference by various respondent doctors, but it points out a target for future continuing medical education programmes.

Regarding myocardial infarction, use of beta-blockers and ACE inhibitors was adequate, but that of ARBs was below expectation. This also reveals a need to improve awareness of the utility of ARBs after myocardial infarction.

An analysis of prescription habits of various zones revealed no significant differences in preference of various drugs for this indication.

DISCUSSION

Angina pectoris is characterized as chest discomfort of short duration (minutes) that is usually retrosternal in location relieved by rest, removal of stress, and/or the administration of nitroglycerin.(1) Approximately of 24% of the male and 26% of the female population of the United States have angina pectoris.

Due to the enhanced myocardial oxygen demand created by increases in blood pressure (BP) –systolic BP (SBP) in particular –and heart rate, hypertensive patients with chronic stable angina are at particular risk of developing complications or symptoms. A study of 25 patients with known CHD who underwent simultaneous electrocardiographic and ambulatory BP monitoring (ABPM) showed that a majority of silent ischemic episodes were preceded by an average increase in SBP of 10 mm Hg, as well as a significant increase in heart rate. (2) Therefore, persons with both stable angina (with or without silent ischemic episodes) and hypertension derive particular benefit from treatment with ß – blockers and calcium blockers (CCBs).

The goal of treating patients with CHD and hypertension are to lower BP, relieve angina, reduce ischemia, and prevent future cardiovascular (CV) events. First –line therapy should be with a ß – blocker without intrinsic sympathomimetic activity unless contraindicated, because these agents are indicated as first –line treatment for both hypertension and CHD. ß –Blockers reduce myocardial oxygen consumption and heart rate and help enhance coronary flow. Thus, they are particularly helpful in reducing angina in the hypertensive patient.

If angina continues on ß – blocker therapy, then long –acting CCBs can be added to the regimen. CCBs decrease total peripheral resistance, which leads to decreases in BP and in wall tension, thus reducing myocardial O_2 consumption. CCBs also decrease coronary resistance and enhance post-stenotic coronary perfusion, which increases myocardial O_2 supply. Although non-hihydropyridine CCBs can be used as anti anginals in combination with a ß- blocker, there is associated risk due to the potential for severe bradycardia and/or heart block.. Therefore, if a CCB is needed in addition to a ß –blocker to control angina in a hypertensive patient, it should be a long –acting dihydropyridine CCB.

The use of angiotensin –converting enzyme (ACE) inhibitors as anti ischemic therapy continues to be controversial. More than 20 studies have examined whether these agents are or are not useful in preventing ischemia, but only two of these included large group of patients. In the Perindopril Therapeutic Safety Collaborative Research group study, 490 hypertensive patients with CVD and/or risk factors for CVD were randomized to treatment with an ACE inhibitor (perindropil) or placebo. Persons in the perindropil group had significantly less ST depression during maximal treadmill exercise testing and fewer anginal episodes ($p<.05$ for both anginal episodes and maximal ST depression).(3) The Quinapril Antischemia and Symptoms of Angina Reduction (QUASAR) trial was a study of 336 patients with stable CHD who were randomized to an ACE inhibitor (quinapril) or placebo. Approximately half of the study population had medically treated hypertension, and all were examined for ischemic events with treadmill testing, ambulatory ECG monitoring, and the Seattle Angina Questionnaire. No significant difference was demonstrated between the two groups either at 8 or 16 weeks.(4) Based on currently available evidence, the use of ACE inhibitors as anti ischemic /antianginal agents is not indicated.

ß –Blockers (nonintrinsic sympathomimetic activity) are first –line agents for both acute MI and hypertension. They help limit infarct size, decrease the risk of recurrent MI, improve survival, and decrease the incidence of sudden cardiac death secondary to fatal arrhythmias.(5,6,7) The dose of ß –blocker should be that which achieve adequate reduction in heart rate and BP while still being tolerated by the patient.

CCBs can be used for acute MI in situations in which ß blocker therapy is inadequately controlling angina , BP, and/or heart rate (e.g, supraventricular tachycardia), or if ß blockers are poorly tolerated or contraindicated. Short –acting dihydropyridine CCBs should be avoided in patients with acute MI, pulmonary edema, or LV dysfunction. (8,9)

ACE inhibitors are indicated in all patients with acute MI who can tolerate them. In a hemodynamically stable (SBP ≥ 90-100 mm Hg) patient post –MI, an oral ACE inhibitor should be initiated, generally within 24 hours of onset of the event, particularly if the infarct is anterior and associated with depressed LV function (LVEF < 40%) and/or heart failure.(10,11)

The large clinical trials have shown that the greatest benefit occurs in patient who are at highest risk (Killip class 2 or 3, heart rate ≥ 100 beats/min). The hemodynamic effects and overall benefit of ACE inhibition are seen early. These findings help support the current recommendations that ACE inhibitors should be initiated routinely after acute MI and continued for an indefinite period.

Angiotensin receptors blockers (ARBs) have been proven to be effective as antihypertensive agents for both hypertension and heart failure and are now used in persons who are ACE inhibitor intolerant or allergic. Emerging data appear to support the use of ARBs in MI.

Two studies conducted in India suggest that physician practice is more in accord with guidance recommendations than most other countries. Survey data of 1076 prescriptions written to patients attending an outpatient hypertension clinic revealed that ß –blockers were the most frequently prescribed (51%), followed by calcium channel blockers (47%) (12). This study did not differentiate between patients with new versus chronic hypertension nor single and combination therapies, and did not assess prescriptions in patients with angina or history of heart attack.

The same pattern emerged in another study (13) of 300 patients attending an internal medicine clinic: ß –blockers were the most frequently prescribed (46.7%), followed by calcium channel blockers (34.3%), and then ACE inhibitors (30%).

Similar findings are seen in the IMPERIAL study, which reveals the encouraging news that Indian doctors are aware of, and follow, current prescription guidelines.

There is not much confusion regarding the drugs of choice in patients with co-existent hypertension and coronary artery disease. Many physicians prefer personal experience, rather than guidelines, as a barometer by which to decide a particular patient's therapy. However, the use of calcium channel blockers in angina, and ARBs after myocardial infarction, may be sub-optimal.

The IMPERIAL study has studied the practices of Indian physicians towards hypertension management in various classes of patients. The study highlights the preferred management approaches followed by our peers while dealing with hypertension. It reveals the awareness of Indian doctors regarding current guidelines on management of hypertension with concomitant coronary artery disease.

The IMPERIAL study reveals preference amongst Indian doctors for both beta-blockers and angiotensin converting enzyme inhibitors after myocardial infarction, and beta-blockers for the management of hypertension with angina. The choice of these two drugs is perhaps due to their perceived benefit of cardioprotection.

At the same time, use of ARBs and calcium channel blockers, arguably the most potent class of antihypertensive drugs, is lower than expected. This discrepancy is difficult to explain, though the reduced use of diuretics may be due to their perceived negative metabolic effects.

LIMITATIONS

The IMPERIAL study has included responses from consulting physicians and cardiologists, from diverse backgrounds. This should be seen as its strength, as it has relied on a cumulative experience of 6217 years of clinical practice, and should not be thought of as a limitation.

In the study, specific questions were not asked regarding preferential use of monotherapy versus combination anti-hypertensive therapy in coronary artery disease. No effort was made to assess prescribing habits in patients with coexistent heart failure, or diabetes, or co-existent nephropathy.

The study did not ask doctors to take into account the influence of age, gender, diabetic status, other co morbid conditions, and socioeconomic status while deciding their prescription.

Other reports from the IMPERIAL study will focus on prescribing habits related to hypertension with renal failure/nephropathy, diabetes and thyroid dysfunction.

CONCLUSION

The IMPERIAL study has shed light on the way in which Indian doctors prefer to treat hypertension in patients with concomitant coronary artery disease. It has tried to fulfil a major, unmet need of physicians, who are confronted frequently with these patients, are confused by the multiple guidelines available, yet do not have access to their colleagues' experience and clinical acumen, to help them plan therapy.

In patients with angina, there was a clear consensus as to the preferred antihypertensive, with most doctors preferring beta-blockers. A similar consensus was noted in favour of ACE inhibitors and beta-blockers both, in patients being treated after myocardial infarction.

These results may form the basis for further debate and discussion, regarding the appropriate management of hypertension in coronary artery disease. The results of the IMPERIAL study also form a basis for discussion and planning further continuing medical education programmes.

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