

EFFICACY OF MONOTHERAPY VERSUS COMBINATION THERAPY IN MODERATE HYPERTENSION

ABID A. KHAN, MAIMOONA INAYAT

SUMMARY

This prospective study was conducted to ascertain the difference in efficacy of a long term ACE inhibitor, Ramipril, used alone and in combination with a dihydropyridine calcium antagonist, amlodipine, in moderate hypertension. The patients were free from long term complications of hypertension. This study included 60 patients aged 25-62 years (42males , 18 females) with essential hypertension, stage II i.e. systolic B.P ³160 mmHg and diastolic B.P³100mmHg (JNCVI). Two groups of patients were formed, group A included patients treated with Ramipril alone and group B included patients treated with combination of Ramipril and amlodipine over a period of six weeks. The study showed a prominent decline in blood pressure of patients in both groups, however target blood pressure was achieved and sustained more effectively in group B .

It is concluded that in order to obtain a more stable drop in blood pressure, combination therapy is more beneficial both in efficacy and cost effectiveness than monotherapy.

Keywords: -

INTRODUCTION

Hypertension is taking an epidemic course world wide including Pakistan.

It remains a common and serious problem, contributing in a major way to the most common causes of morbidity and mortality in the developing societies¹. As a consequence of the increased awareness of the damage caused by hypertension and with the recognition that the progress of hypertension induced cardiovascular diseases, cerebrovascular and renovascular diseases can be slowed , if not stopped by its treatment ², the management of hypertension is now second only to upper respiratory tract infections as an indication for visit to the physician in the United States ³ . A number of anti- hypertensives are available world wide, but ACE inhibitors are on the lead.

The first one captopril introduced in 1981, was used ubiquitously, due primarily to its beneficial effect on both systolic and diastolic blood pressure ⁴.By dilating capacitance vessels without significantly

affecting cardiac output, it proved effective both in hypertension and cardiac failure ⁵. As it was short acting and to be given atleast three times a day which slightly affected the patient compliance to the drug , a new class of ACE inhibitors were introduced which were equally effective and are long acting, given once a day with good patient compliance. One such drug of this class,Ramipril, has proved to be effective, long acting, with good patient compliance, least side effects and reasonably accepted as a monotherapy⁶. The present study was conducted to examine the efficacy of Ramipril, 5 mg, (long acting ACE inhibitor) on hypertensive population of moderate degree and to compare its efficacy as monotherapy versus combination therapy (amlodipine, 2.5 mg with Ramipril 5 mg).

PATIENTS AND METHODS:

60 patients aged 25- 62 years (42males , 18 females) with essential hypertension ,stage II i.e. systolic B.P ³160 mmHg and diastolic B.P³100mmHg (JNCVI) were evaluated in the study .

Ramipril was given 5mg once a day as a monotherapy in group A. Those who were put on combination

* *Bolan Medical Complex Hospital ,Department of Cardiology ,Quetta*

therapy (Ramipril 5 mg with amlodipine 2.5 mg) were categorized as group B. The study was open and uncontrolled. Arterial blood pressure was measured with sphygmomanometer by same observer. An average of three readings in supine position after 5-10 minutes rest was obtained and the reading after 2 minutes in erect posture was obtained in each patient at the time of inclusion.

Each patient was subjected to 12 lead E.C.G. Measurement of blood pressure was performed two weekly for 6 weeks , at the same time of the day .

INCLUSION CRITERIA.:

Patients with known essential hypertension and newly diagnosed hypertension were included. To keep the baseline values of blood pressure unbiased, all types of antihypertensives were stopped, in the pretreated patients, for atleast one week prior to the trial.

EXCLUSION CRITERIA:

Secondary hypertension, myocardial infarction in the preceding 6 months, cardiac failure, renal failure, advanced degree heartblock, severe hepatic insufficiency and pregnancy were excluded from the population under study.

RESULTS:

The study included 60 patients with moderate hypertension. 18 patients were male and 42 females, as shown in fig 1 , aged between 28 years to 62 years, mean age 45 ± 12 years . Mean weight was 68 ± 3 kg (range between 56- 85 kg). There were no drop outs.

The effects of ramipril as a monotherapy (5.0 mg) and when combined with other anti hypertensives (amlodipine,2.5mg with 5 mg ramipril) was studied in two groups of patients (20 patients on monotherapy & 40 patients on combination therapy). It is evident after monitoring their blood pressures after 2 , 4 and 6 weeks that combination therapy (Ramipril 5 mg +amlodipine 2.5 mg) was more beneficial, in bringing down blood pressure, both diastolic and systolic to a greater degree than monotherapy with Ramipril 5 mg(see fig 3 & 4).

Though monotherapy with Ramipril decreased blood pressure more rapidly, combination therapy produced consistent and more stable decrease in blood pressure over a period of 6 weeks (see fig 2& 3). None of the patients reported new onset of cough after commencing therapy.

The average fall of blood pressure with monotherapy after 6 weeks was 23.1 mmHg systolic and 12.15 mmHg diastolic, while combination therapy produced a net fall of 47.6 mmHg systolic and 18.1mmHg diastolic over the same period ($p < 0.005$). Combination therapy also had an edge over monotherapy in cost effectiveness.

Figure - 1
male to female ratio in 60 patients under study.

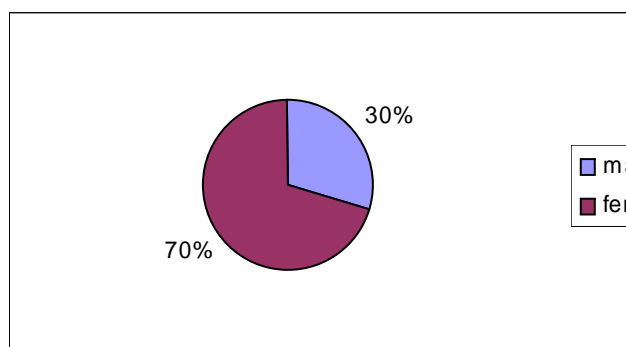


Figure - 2
levels of systolic and diastolic blood pressure at baseline to 6 weeks in group B(combination therapy)

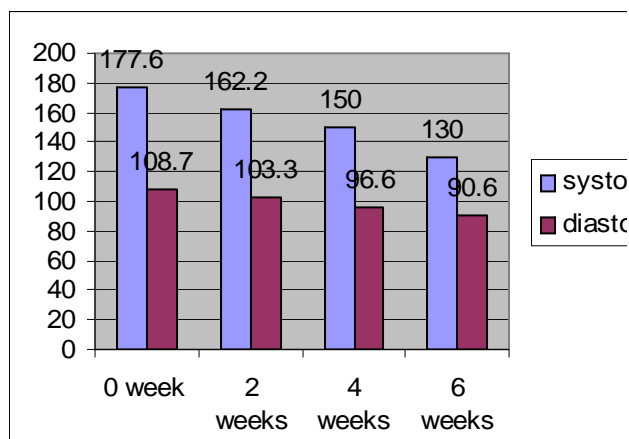


Figure - 3
Levels of systolic and diastolic blood pressure in group A (monotherapy).

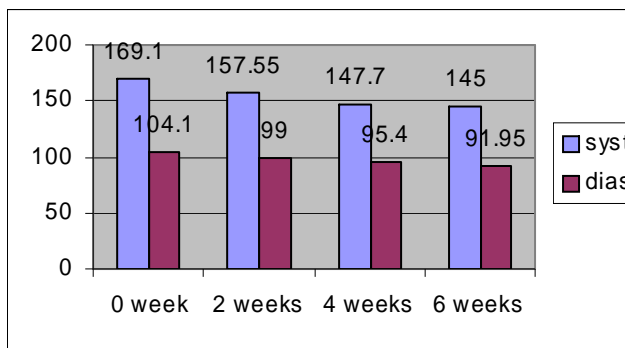


Figure - 4
Comparison of levels of systolic blood pressure in group A and group B (p<0.005).

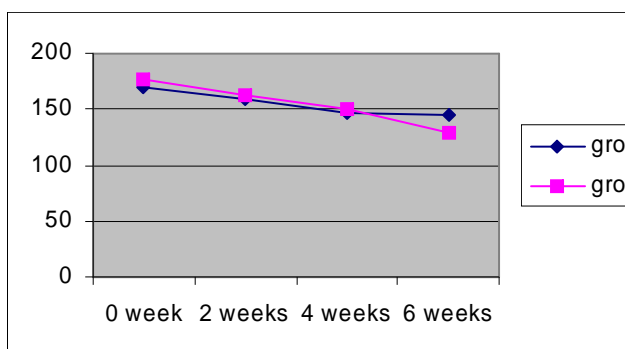
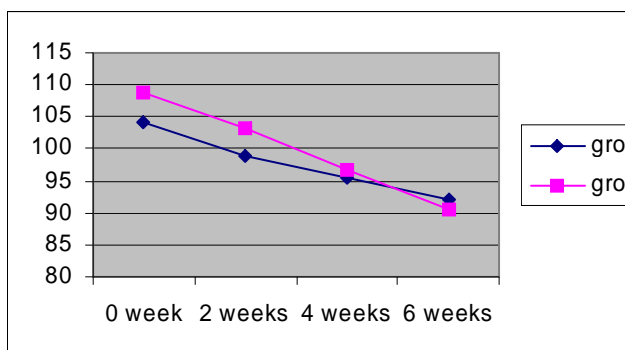


Figure - 5
Comparison of levels of diastolic blood pressure in group A and group B (p<0.005).



DISCUSSION :

A number of studies have been published on combination therapy for the treatment of hypertension. One such combination, ACE inhibitors with diuretics, proved to be very effective in reducing blood pressure to the desired level 7, but the diuretic

constituent due to its negative metabolic effect on serum lipids, uric acid and blood glucose, may produce adverse effects⁸. ARB's with diuretic also forms a good combination⁹. Another potent combination available in the market is a non-dihydropyridine, calcium antagonist, verapamil, with ACE inhibitor, trandolopril, a good choice in a high risk hypertensive patient with coronary artery disease. Beta blocker with ACE inhibitors have been used widely in combination in selected population, limiting its use in diabetic hypertensives⁸.

ACE inhibitors have long been hailed as the most effective anti hypertensives, owing to their ability to intercept the major pathway of renin-angiotensin system, which plays an important role in the pathogenesis of essential hypertension². Having the ability to actively inhibit the production of angiotensin, these drugs have evolved to produce long term effects not only on blood pressure control but also in counteracting the ill effects of long standing hypertension. Ramipril has been shown in lowering blood pressure in all groups of hypertensives, including those with diabetes, proteinuric nephropathy, left ventricular hypertrophy and atherosclerosis¹⁰. Effective as it is alone, the drug has been shown to have greater efficacy when combined with amlodipine¹¹. Such a combination has proved to be effective in reducing blood pressure to a target level, better tolerability, good patient compliance and produces minimal side effects.

CONCLUSION:

Ramipril is an effective ACE inhibitor in reducing blood pressure in hypertensive subjects. The drug is well tolerated, long acting, can be used effectively in uncomplicated hypertensives and is well prescribed in patients with comorbid conditions like coronary artery disease, diabetic hypertensives, left ventricular hypertrophy and left ventricular failure. The combination of Ramipril with small dose Amlodipine proved effective in achieving goal blood pressure.

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