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RESEARCH ARTICLE

DOSE TITRATION OF CONCURRENT USE OF TWO ANTIHYPERTENSIVES IN A TERITARY CARE SUPERSPECIALITY HOSPITAL

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ABSTRACT

Ramipril is an angiotensin converting enzyme (ACE) inhibitor and Metoprolol a β-adrenergic blocker used as antihypertensive. In this study we aimed to titrate the concurrent use of two most conventionally used antihypertensives. Objectives of this study were to evaluate the effect of regular intake of Ramipril and Metoprolol by patients with mild to moderate grade of hypertension, to adjust the dose and to educate the patients by providing patient counseling. In this multidose open label randomized block study, was conducted between March 2010 and November 2010 at CARE super specialty hospital, Hyderabad. A total of 60 patients were enrolled and were asked to have total of four visits including first screening visit, with 6 weeks interval between each visit. Study treatments included; Dose A (2.5mg Ramipril+25mg Metoprolol), Dose B (5mg Ramipril+50mg Metoprolol) and Dose C (10mg Ramipril+50mg Metoprolol) and patient counseling emphasizing on the role of diet, life style modification and regular exercise for management of hypertension. Blood pressure (B.P) was measured on every visit including the day of enrolment and the results were analyses from the data obtained. The study concluded that gradual up-gradation of the combination dose was useful in controlling hypertension. Along with it, patient counseling was found to be beneficial for the patients.

INTRODUCTION

Hypertension is a condition where a systolic blood pressure ≥ 140 mmHg either/or diastolic blood pressure ≥ 90mmHg. It occurs when excessive force is exerted against artery walls as the heart pumps blood. Hypertension is called a silent killer, because it has no symptoms until it has reached an advanced stage and currently there is no cure. It is classified as either primary (essential) or secondary. About 90–95% of cases are termed "primary hypertension", which refers to high blood pressure for which no medical cause can be found. The remaining 5–10% of cases (Secondary hypertension) are caused by other conditions that affect the kidneys, arteries, heart, or endocrine system (Kosugi *et al.,* 2009; Dickson and Sigmund 2006). Ramipril is a drug used in the treatment of hypertension. It is an Angiotension conversion Enzyme (ACE) inhibitor. ACE inhibitors reduce the production of Angiotensin II slowly which will help to relax the arteries in the muscles. Also, by dilating arteries, Ramipril allows the passage of more blood to the heart (Dodt *et al.,* 2009). Metoprolol is a beta-adrenergic blocking agent that is used for treating high blood pressure. It reduces the force of contraction of heart muscle and thereby lowers blood pressure. By reducing the heart rate and the force of muscle contraction, Metoprolol reduces the need for oxygen by heart muscle (High blood pressure causes 2010; Chobanian *et al.,* 2003). Apart from using pharmacological treatment, non-pharmacological treatment such as; dietary sodium restriction, smoking cessation, moderate alcohol consumption, DASH (Dietary Approaches to Stop Hypertension) diet and exercise helps patients to control hypertension (Carretero and Oparil 2000). Patient counseling is also an important factor which improves patient's knowledge and attitude towards the disease which improves better control of hypertension. (Klabunde and Richard 2007).

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Aim and Objectives

In this study we aimed to titrate the concurrent use of two most conventionally used antihypertensive in a tertiary care superspeciality hospital. Objectives of this study were to evaluate the effect of regular intake of ramipril and metoprolol by patients with mild to moderate grade of hypertension, to adjust the dose and to educate the patients by providing patient counseling.

MATERIALS AND METHODS

In this multidose open label randomized block study, conducted between March 2010 and November 2010 at CARE super specialty hospital, Hyderabad. A total of 60 subjects with age group of 30 to 60 years were enrolled after getting written consent and were asked to have total of four visits including first screening visit, with 6 weeks interval between each visit.

1. Screening visit or visit 1 (week 0) drug dispensing.
2. visit 2 (6 weeks)

3. visit 3 (12 weeks)
4. visit 4 (18 weeks)

Study treatments included combination doses of ramipril and metoprolol in 3 different dosage strengths viz; DOSE A (2.5mg ramipril + 25 mg of metaprolol), DOSE B (5mg of ramipril + 50 mg of metaprolol) and DOSE C (10 mg of ramipril + 50mg of metaprolol). Patient counseling were provided on each visit emphasizing on role of diet, life style modification and regular exercise for management of hypertension. All the enrolled subjects were followed up every six weeks and were updated to next regimen depending upon the response.

RESULTS AND DISCUSSION

Gender distribution of study population shows that out of 60 patients included in the study, 20 were females (33%) and 40 were males (67%). Comparing to Females, more number of Males are suffering with Hypertension. (Table 1 and Fig.1)

Table 1. Gender distribution of study population

Gender	No of Patients	Percentage
Males	40	67
Females	20	33

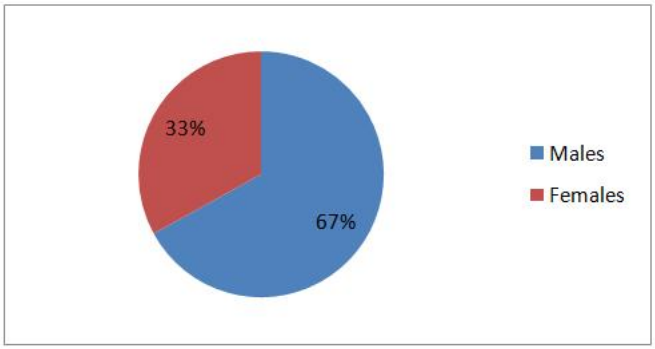

Figure 1. Gender distribution of study population

Age distribution of study population shows that majority of the people affected by the hypertension fall in to the category of 41-50 years (50%) of age group followed by 51-60 years (33%) and then 30-40 years (17%) (Table 2 and Fig.2)

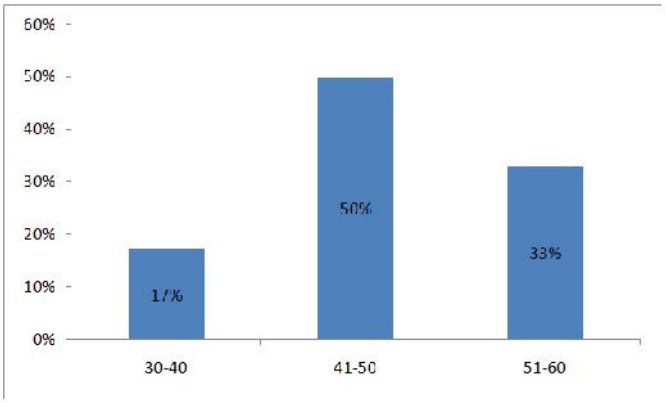

Figure 2. Age distribution of study population

Table 2. Age distribution of study population

Age Group	No. of Patients	Percentage
30-40	10	17
41-50	30	50
51-60	20	33

Personal habits of study population shows that personal habits like smoking and drinking can increase the risk of getting hypertension. It shows that majority of the people affected by the hypertension fall in to the category of Smoking (8%) and drinking (25%) and then Smoking and Drinking (33%). (Table 3 and Fig.3)

Table 3. Personal habits of study population

Personal Habits	No. of Patients	Percentage
Smoking	5	8.33
Drinking	15	25
Smoking and Drinking	20	33.33

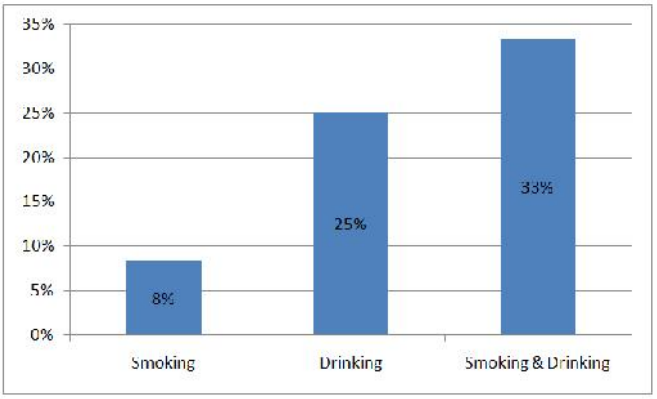

Figure 3. Personal habits of study population

Food Habits of study population shows that a person who takes high calorie diet (Non-Veg food habits) are at higher risk of getting hyper tension. (Table 4 and Fig.4)

Table 4. Food habits of study population

Food Habits	No. of Patients	Percentage
Veg	20	33.33
Non-Veg	40	66.66

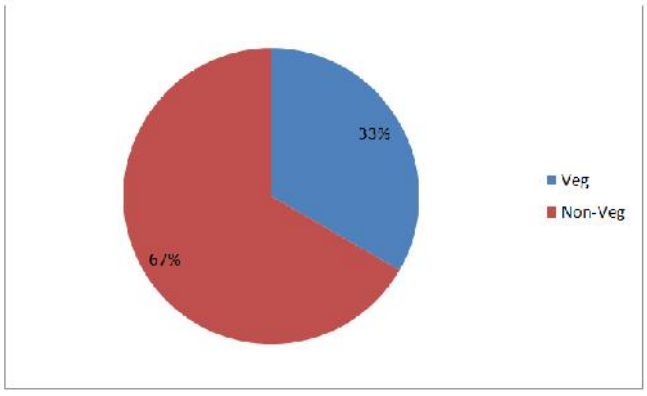

Figure 4. Food habits of study population

Life Style pattern of study population shows that people who have sedentary life style are at higher risk of getting hypertension. (Table 5 and Fig.5)

Table 5. Life Style pattern of study population

Life Style	No. of Patients	Percentage
Moderate	25	41.66
Sedentary	35	58.33

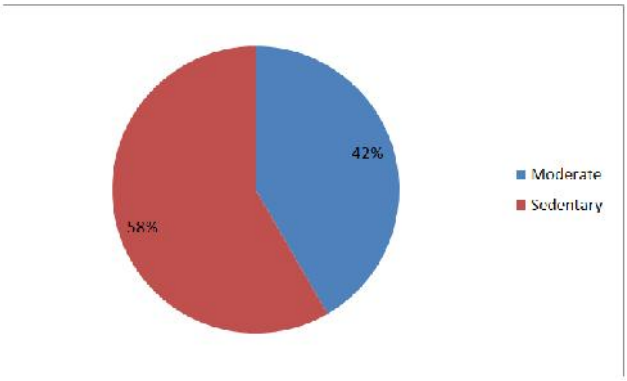

Figure 5. Life Style pattern of study population

Comorbid conditions of study population shows the number of patients who have comorbid conditions other than Hypertension 58% which include diabetes 25% and hyperthyroidism 16%. (Table 6 and Fig.6)

Table 6. Co morbid conditions of study population

Comorbid Conditions	No. of patients	Percentage
Hyper tension	35	58.33
Hypertension and Diabetes	15	25.00
Hypertension and Hyperthyroidism	10	16.66

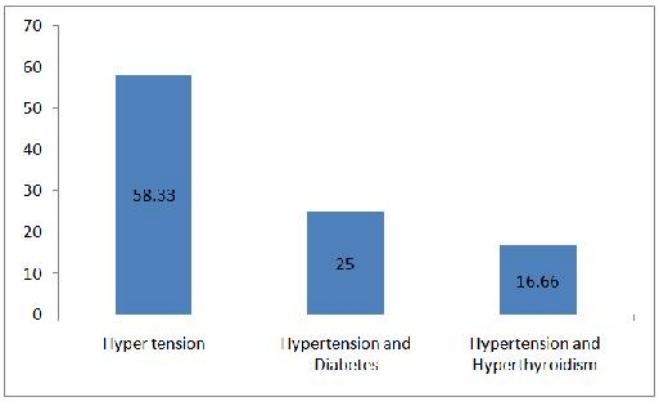

Figure 6. Co morbid conditions of study population

Side effects of the treatment shows these drugs are already proved to be safe drugs and hence side effects are mild. (Table 7 and Fig.7)

Table 7. Side effects of the treatment

Side effects	No. of Patients	Percentage
Diarrhoea	2	3.33
Constupation	2	3.33
Dizziness	1	1.66

In second visit a significant decline in blood pressure (BP) was observed with most of the subjects. In 30 subjects, BP has been even come to near normal level.

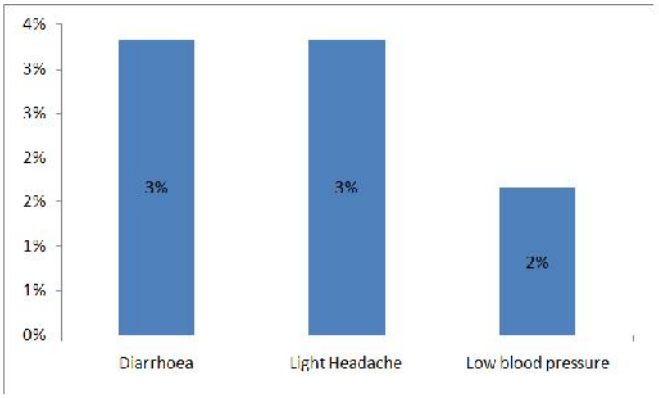

Figure 7. Side effects of the treatment

Out of rest 30 subjects, 20 subjects upgraded to dose B [5 mg ramipril+50 mg metoprolol] and remaining 10 subjects have been continued with same Dose A. In third visit a significant decline in BP is observed in most of the subjects. A total of 55 subjects had their blood pressure around near normal level. Remaining 5 subjects were given Dose C [10mg ramipril+50mg metoprolol] and in fourth visit, all 60 subjects reached the targeted near normal BP level. (Table 8 and Fig.8)

Table 8. Average B.P in each visit

Visits	Systolic Blood Pressure	Diastolic Blood Pressure
VISIT 1	144.83	98.17
VISIT 2	135.33	91.50
VISIT 3	128	85.33
VISIT 4	122.67	81.67

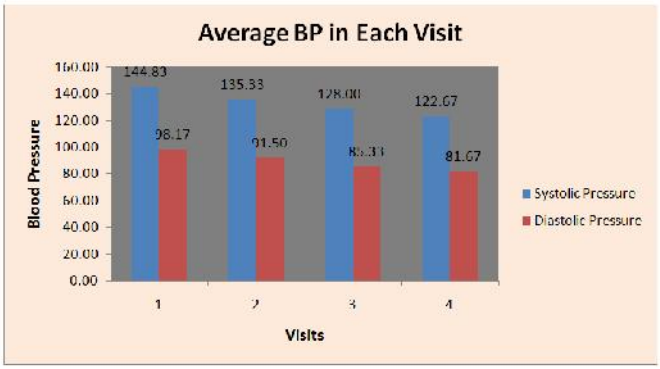

Figure 8. Average B.P in each visit

Patient counseling were also found to be beneficial which improves patients knowledge and attitude towards disease and helps in better control of BP.

Summary and Conclusion

This study is on treatment compliance with antihypertensive drugs and physician's follow up visits compliance, and its efficiency in lowering blood pressure in patients with hypertension. Total 60 patients were included in this study. All of them treated with Ramipril and metaprolol combination drug

therapy in 3 dosage regimens up to 6 weeks depending up on their blood pressure response in each visit. The patient has paid 4 visits with duration of 15 days each. In each visit blood pressure was measured. It should be known whether the patient is taking medication regularly or not, to detect this drug accountability has been check in each of the patient's visit. Out of 60 patients, the dosage regimen has been upgraded in 30 patients. Out of 60 patients only 4 patients have fallen in irregularity in taking medication. No patients have failed to attend the physician follow up visits as scheduled. Out of 60 patients only 4 patient's BP has not come to normal even after the 4 visits. Only few adverse events were observed during whole study. They are headache, anorexia and dry cough. Finally, the results showed that 90 % of the hypertension patients have attained the normal blood pressure when they all have taken medication regularly and attended the physician's follow up visits as scheduled.

REFERENCES

Barreto AC, Maeda NY, Soares RP, Cícero C, Lopes AA. Rosuvastatin and vascular dysfunction markers in pulmonary arterial hypertension: a placebo-controlled study. *Braz J Med Biol Res*. 2008; 41:657–663.

Carretero OA, Oparil S. "Essential hypertension. Part I: definition and etiology (January 2000).

Dickson ME, Sigmund CD. "Genetic basis of hypertension: revisiting angiotensinogen". *Hypertension* (July 2006) .

Dodt C, Wellhöner JP, Schütt M, Sayk F (January 2009). "(Glucocorticoids and hypertension)" (in German).

Esler M, Jennings G, Lambert G. Noradrenaline release and the pathophysiology of primary human hypertension. *Am J Hypertens* 1989;2:140S-146S.

High blood pressure causes. American Heart Association. Accessed (June 8, 2010).

Ierszenbaum, Abraham L. Histology and cell biology: an introduction to pathology. Mosby Elsevier. (October 2007).

Jatoi NA, Jerrard-Dunne P, Feely J, Mahmud A. Impact of smoking and smoking cessation on arterial stiffness and aortic wave reflection in hypertension. Hypertension. 2007; 49: 981–985.

Klabunde, Richard E. "Cardiovascular Physiology Concepts - Mean Arterial Pressure". (May 2007).

Kosugi T, Nakagawa T, Kamath D, Johnson RJ. "Uric acid and hypertension: an age-related relationship?". *J Hum Hypertens* (February 2009).

Meaume S, Benetos A, Henry OF, Rudnichi A, Safar ME. Aortic pulse wave velocity predicts cardiovascular mortality in subjects >70 years of age. Arterioscler Thromb Vasc Biol. 2001; 21: 2046–2050.

Millasseau SC, Stewart AD, Patel SJ, Redwood SR, Chowienczyk PJ. Evaluation of carotid-femoral pulse wave velocity: influence of timing algorithm and heart rate. Hypertension. 2005; 45: 222–226.

Rich S, Kaufmann E, Levy PS. The effect of high doses of calcium-channel blockers on survival in primary pulmonary hypertension. *N Engl J Med*. 1992;327:76–81.

Schlaich MP, Lambert E, Kaye DM, et al. Sympathetic augmentation in hypertension: role of nerve firing, norepinephrine reuptake, and angiotensin neuromodulation. Hypertension 2004;43:169-175.

Wade M. Intravenous treprostinil in pulmonary arterial hypertension: a controlled trial in India. Chest. 2007;132:635b–636.

Worth H, Siemons H, Rubo J, Goeckenjan G, Loogen F. Acute and chronic effects of molsidomine on gas exchange and hemodynamics in patients with primary vascular pulmonary hypertension. Prax Klin Pneumol. 1987;41:598–599.

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