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Original Research Article

Prospective, randomized double blind comparative study of safety and efficacy of carvedilol versus atenolol in patients of mild to moderate hypertension

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ABSTRACT

Background: Carvedilol is a new cardiovascular compound with the combined pharmacologic properties of nonselective ß-blockade and vasodilation. The Aim of the study was to compare the safety and antihypertensive efficacy of 25mg Carvedilol once daily with 50mg atenolol once daily in patients with mild to moderate essential hypertension.

Methods: This was a single center study conducted in Rangaraya Medical College, Kakinada. 80 eligible patients with mild to moderate hypertension were randomized to receive 25mg Carvedilol once daily (40 patients) or 50mg atenolol (40 patients) in a double-blind 12-week treatment phase. At each visit 0, 4, 8 and 12 weeks of treatment, sitting Blood Pressure (BP) and heart rate were measured. The effect on BP reduction within the group is compared by paired "t"test and the effect on reduction of BP between two study groups compared by unpaired "t"test.

Results: After 12 weeks of treatment, the mean reduction of SBP (Systolic Blood Pressure) with carvedilol is 22.33±8.31mmHg with no Significant difference (p >0.05) compared to atenolol group mean reduction in SBP of 21.37±10mm Hg. The mean reduction in DBP (Diastolic Blood Pressure) after completion of the study in carvedilol group is 6.75±4.82mm Hg with no Significant difference (p >0.05) compared to atenolol group mean reduction in DBP of 8.55±5.25mm Hg. No significant difference seen in the efficacy parameters of both the drugs. The incidence of adverse effects such as bradycardia, headache, nausea, vomiting, hypotension and rash is less with carvedilol.

Conclusions: In patients with mild to moderate hypertension, there was no statistically significant difference between efficacy of carvedilol or atenolol with regard to the degree of reduction in BP or the percentage of patients achieving a response to therapy but carvedilol showed a better safety profile when compared to atenolol.

Keywords: Atenolol, Blood pressure, Carvedilol, Essential hypertension

INTRODUCTION

Hypertension is emerging as a serious public health problem in developing countries. The prevalence of hypertension increases with advancing age. About 50%

of people between the age of 60-69 years old have hypertension and the prevalence is further increased beyond age 70.[1] Elevated arterial pressure causes pathological changes in the vasculature and hypertrophy of the left ventricle. Hypertension doubles the risk of cardiovascular disease, including coronary heart disease (CHD), congestive heart failure (CHF), ischemic and hemorrhagic stroke, renal failure, peripheral arterial disease.[2] Increasing awareness and diagnosis of hypertension and improving control of blood pressure with appropriate treatment are considered critical public health initiatives to reduce cardiovascular morbidity and mortality.[3] Hypertension is the most prevalent chronic disease in India with prevalence increasing rapidly both in urban and rural population.[4] The prevalence of hypertension ranges from 20-40% in urban adults and 12-17% among rural adults. The number of people with hypertension is projected to increase from 118 million in 2000 to 214 million in 2025.[5] In India, 23.10% men and 22.60% women over 25 years old suffer from hypertension. It is released in may 2012 by WHO global health statistic 2012. Recent studies show that for every known person with hypertension in India, there may possibly be 2 persons with undiagnosed hypertention or prehypertension. With over 139 million patients, India accounts for 15% of worlds uncontrolled hypertension patients.[6] Carvedilol is a new cardiovascular compound that exhibits two main pharmacologic properties at therapeutic doses. It is a nonselective, competitive ß-adrenoceptor antagonist with no intrinsic sympathomimetic activity.[7]

Central to its antihypertensive effect is a reduction in total peripheral resistance mediated by competitive α-adrenoceptor blockade. Clinical trials in patients with essential hypertension have shown 25 to 100 mg Carvedilol once daily to be a safe and effective antihypertensive dosing regimen. Carvedilol also has demonstrated calcium channel blocking actions at higher concentrations in preclinical models, which may contribute to increasing blood flow in certain vascular beds.[8]

Atenolol, a cardio selective ß-blocking agent, is indicated for the treatment of essential hypertension at the recommended dosage of 50 to 100 mg once daily. The purpose of this study was to compare the safety and antihypertensive efficacy of 25 to 50 mg Carvedilol once daily with 50 to 100 mg atenolol once daily in patients with mild to moderate essential hypertension.[9]

METHODS

The protocol for the study was approved by the Dr. N.T.R University of Health Sciences, Vijayawada Andhra Pradesh. According to JNC 7 classification. Basing on the inclusion criteria, patients of both sexes aged between 20 to 65 years attending medical out-patient department in the Government General Hospital, Kakinada, with newly diagnosed and untreated mild to moderate hypertension i.e. 120-139/ 80-89mmHg as mild/ prehypertension and 140-159/ 90-99mmHg as moderate/ stage 1 hypertension, a total of 126 patients were selected. Among 126 patients, 46 were excluded basing on exclusion criteria, which includes, the patients who are irregular in study groups, who are on concurrent therapy with other medications, those who are suffering with other comorbidities and those who were not willing to give consent. A total of 80 patients were enrolled in the study as per the selection criteria and randomly allocated to two groups with 40 patients each. Group A- n=40 who received Carvedilol 25mg Once daily morning dose and Group B- n=40 who received Atenolol 50mg Once daily morning dose. Both the group patients were treated for 12 weeks and following were assessed at 0, 4, 8 and 12 weeks.

- Complete blood picture, Blood Urea, Serum Creatinine, Serum glutamic oxaloacetic transaminase (SGOT), Serum Glutamic Pyruvic Transaminase (SGPT) Aspartate aminotransferase (AST), Alanine aminotransferase (ALT) are better instead of Serum glutamic oxaloacetic transaminase (SGOT), Serum Glutamic Pyruvic Transaminase (SGPT) and analysis of urine for - Albumin, Sugar and Microscopy.
- ECG**,** recording of blood pressure (Average of three readings of blood pressure was taken in only sitting position as mentioned in methods in introduction with gap of 2 minutes in between each recording), heart rate.
- Side effects of the drugs

Statistical analysis

The data was presented as mean±SD. The effect on blood pressure reduction within the group was compared by paired "t" test and the effect on reduction of blood pressure between two study groups was compared by unpaired "t" test.

RESULTS

In the present study, the number of patients in the age group 41-50 years are the highest consisting of 19 (47.5%) patients in group A and in the age group 51-60 years are the highest consisting of 15 (37.5%) patients in group B.

Table 1: Distribution of age of patients in each study group.

Age in years	Group A	Group B
21-30	0	0
31-40	8(20%)	8(20%)
41-50	19(47.5%)	12(30%)
51-60	9(22.5%)	15(37.5%)
>60	4(10%)	5(12.5%)
Total	40	40

In the present study the percentage of males enrolled is 71.2% and that of females is 28.8% with mild to moderate hypertension.

In the present study the reduction of mean systolic blood pressure (mmHg) after completion of the study in group A and group B are 22.33±3.44 and 21.35±4.26 respectively, with no significant difference in their reduction (p>0.05) (Table 2).

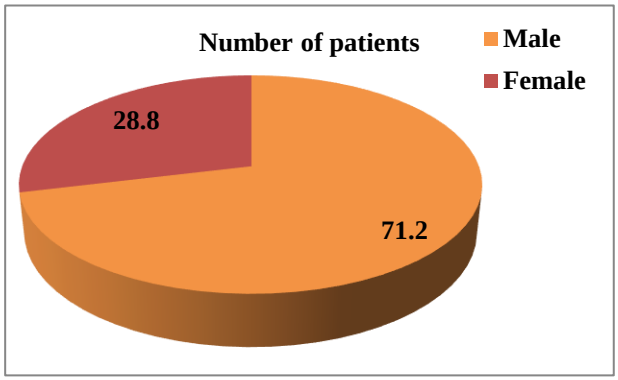

Figure 1: Distribution of gender in the study.

Table 2: Systolic blood pressure in between two study groups.

Duration of therapy	Group A (Mean±SD)	Group B (Mean±SD)
At base line	148.75±7.91	148.35±8.94
4 weeks	135.05±6.33	136.47±7.56
8weeks	128.85±6.57	127.37±4.11
12weeks	126.42±4.47	127±4.68

In the present study the reduction of mean diastolic blood pressure (mmHg) after completion of the study in group A and group B are 6.75±1.69 and 8.55±1.18 respectively, with no significant difference (p>0.05).

Table 3: Reduction in diastolic blood pressure in between two study groups.

Duration of therapy	Group A (Mean±SD)	Group B (Mean±SD)
At base line	90.25±4.10	91.97±3.99
4 weeks	83.572±2.87	85.10±2.85
8 weeks	83.37±2.49	83.67±3.00
12 weeks	83.5±2.41	83.42±2.809

Table 4: Mean heart rate (beats/min) in between two study groups.

Duration of therapy	Group A (Mean±SD)	Group B (Mean±SD)
At base line	80.7±2.80	82.65±2.78
4 weeks	77.9±4.21	80.32±3.24
8 weeks	77.55±4.26	79.6±2.72
12 weeks	75.12±5.17	63.55±8.71

In the present study the reduction in mean heart rate (beats/min) after 12 weeks of the study in group A and group B are 5.58±2.37 and 19.1±5.93 respectively, showed significant difference (p <0.05).

In the total study, bradycardia is seen in 7.5% (3) patients in group A and 15% (6) patients in group B. Headache is seen in 10%(4) patients in group A and 15%(6) patients in group B. Nausea is seen in 5% (2) patient in group A and 10% (4) patient in group B. Vomiting is seen in 2.5% (1) patients in group A and 10% (4) patients in group B. Dizziness is seen in 10% (4) patients in group A and 5% (2) patients in group B. Rhinitis is seen in 2.5% (1) patients and insomnia is seen in 5% (2) patients in group A only. Rash is seen in 2.5% (1) patients and Hypotension is seen in 2.5% (1) patients in group B only.

Table 5: Occurrence of side effects (safety parameters) in both groups.

Side effect	Group A (carvedilol 25mg)	Group B (atenolol 50mg)
Bradycardia	3(7.5%)	6(15%)
Headache	4(10%)	6(15%)
Nausea	2(5%)	4(10%)
Vomiting	1(2.5%)	4(10%)
Dizziness	4(10%)	2(5%)
Insomnia	2(5%)	0
Rhinitis	1(2.5%)	0
Hypotension	0	1(2.5%)
Rash	0	1(2.5%)

Table 6: Descriptive statistics for selective laboratory measurements (liver function tests, renal function tests).

Laboratory parameter	Group A (carvedilol 25mg)		Group B (Atenolol 50mg)	
	Baseline	Endpoint	Baseline	Endpoint
Liver function test				
ALT(U/L)	17.9	17.7	18.6	18.2
AST (U/L)	16.6	16.2	17.2	16.4
Renal function test				
Serum creatinine (mg/dL)	0.8	1	0.9	0.7
Blood urea (mg/dL)	14	14.6	16	16.4

Liver function tests (ALT and AST), renal function tests (Table 6), ECG findings, Complete haemogram and urine analysis at enrollment and during assessment at 4th ,8th and 12 weeks (end of study) were normal and no abnormality detected for both the drugs.

DISCUSSION

High blood pressure (BP) is a major public health problem in India and elsewhere. The impact of hypertension on highly vascular organs such as kidney

can be particularly devasting. In India hypertension is solely responsible for majority of deaths due to stroke and coronary heart diseases.[10] Prospective Studies Collaboration has reported that reducing BP can substantially decrease cardiovascular risk.[11] Anti hypertensives contribute in a major way in reduction of hypertension associated complications.

In the present study the number of patients in the age group 41-50 years are the highest consisting of 19 (47.5%) patients in group A and in the age group 51-60 years are the highest consisting of 15 (37.5%) patients in group B and there were 71.2% male patients and 28.8% female patients which were similar to study done by Luis M. Ruilope.[7] Previous studies[7,13] have compared the effects of carvedilol and atenolol on haemodynamic parameters in patients of mild to moderate essential hypertension. Like our study, there were no significant differences between the effects of carvedilol and atenolol on systolic and diastolic blood pressures during treatment. But the mean Heart Rate in present study showed significant difference ($p<0.05$) between group A and group B which is in contrast to previous studies.[7,13]

Our study showed dizziness (10%) and headache (10%) were more common with carvedilol similar to that of Luis M. Ruilope study.[7] But bradycardia (15%) and headache (15%) were common with atenolol. Carvedilol and atenolol were equally effective and well-tolerated like widdman L study.[14]

CONCLUSION

Carvedilol is as effective as Atenolol in reducing systolic and diastolic blood pressure. The incidence of adverse effects such as bradycardia, headache, nausea, vomiting, hypotension and rash is less with carvedilol. Both the study drugs are equally effective in reducing the blood pressure but carvedilol showed a better safety profile when compared to atenolol.

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Ethical approval: The study was approved by the Institutional Ethics Committee of Rangaraya Medical College, Kakinada

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