

ORIGINAL RESEARCH

A Comparative Study of Efficacy & Tolerability of Atenolol versus Nebivolol in Patients of Stage I Hypertension

¹Dr. Ashish Puri, ²Dr. Balbir Kaur, ³Dr. Ena Bhajni, ⁴Dr. Parveen Gupta

¹Associate Professor, Dept. Of Pharmacology, Maharishi Markandeshwar College of Medical Science & Research, Sadopur, Haryana.

²Associate Professor, Dept. Of Pharmacology, Adesh Medical College & Hospital, Shahabad, Haryana.

³Assistant Professor, Dept. Of Pharmacology, Maharishi Markandeshwar College of Medical Science & Research, Sadopur, Haryana.

⁴Professor, Dept. Of Medicine, Maharishi Markandeshwar University, Ambala, Haryana.

Correspondence Author

Dr. Balbir Kaur

Associate Professor, Dept. Of Pharmacology, Adesh Medical College & Hospital, Shahabad, Haryana.

E-Mail Id: balbirkaur.123@gmail.com

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ABSTRACT:

Background & Objectives: Hypertension is a major public health problem. It is one of leading causes of death & disability worldwide & a major risk factor for cardiovascular diseases. Nebivolol a 3rd generation beta blocker with high selectivity for β_1 adrenergic receptors also causes vasodilatation by nitric oxide pathways. This dual mechanism of Nebivolol reduces heart rate, BP & improves systolic & diastolic function. Therefore we evaluated the effect and safety of Nebivolol 5 mg once daily against Atenolol 50 mg once daily in patients with stage I hypertension.

Methods: This study comprised of 60 patients of Stage I hypertension. 60 patients in age group of 18-70 years were assigned into two groups. First group of 30 patients administered Tablet Atenolol 50 mg once daily & second group included 30 patients administered Tablet Nebivolol 5 mg once daily. Patients were evaluated at the beginning (baseline) & then at 2, 4, 8, and 12 weeks for BP reduction and adverse effects, if any.

A comparative, prospective, open labeled, parallel group study was conducted at medicine department, MMIMSR, Mullana, Ambala. 60 patients in age group of 18-70 years were randomly assigned into two groups first comprising 30 patients administered Atenolol 50 mg oral once daily & second group also comprising 30 patients administered Nebivolol 5 mg oral once daily. Patients not responding to treatment in both the groups would be put on Amlodipine 2.5 -5mg oral once daily. Patients were evaluated at the beginning & then at 2, 4, 8, and 12 weeks for BP reduction and adverse effects, if any.

RESULTS: At 12 weeks, both groups showed significant ($P < 0.001$) reduction in B.P from baseline. Mean SBP was reduced from 150.07 ± 6.84 mm Hg to 130.87 ± 2.72 mm Hg (Atenolol) and 153.27 ± 5.99 mm Hg to 128.40 ± 4.36 mm Hg (Nebivolol) after 12 weeks treatment (percentage difference was 12.79%, 16.22%). Mean DBP was reduced from 93.00 ± 3.17 mm Hg to 80.33 ± 2.37 mm Hg (Atenolol) and 94.88 ± 2.57 mm Hg to 80.00 ± 2.58 mm Hg (Nebivolol) after 12 weeks treatment (percentage difference was 13.62%, 15.68%).

CONCLUSION: Both the groups were well tolerated and equally effective in reducing blood pressure and heart rate. All reported adverse effects were mild and did not require any alteration or discontinuation of treatment.

KEY WORDS: Atenolol, Nebivolol, SBP, DBP, Hypertension

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INTRODUCTION:

Hypertension means elevated blood pressure which is defined as systemic blood pressure of 140/90 mmHg or more on two separate occasions measured at least one to two weeks apart. The elevation in blood pressure can

be divided into three classes of hypertension. Pre-hypertension describes blood pressure measurements greater than 120 mmHg systolic or 80 mmHg diastolic & less than 139 mmHg systolic or 89 mmHg diastolic. The second classification of hypertension is (stage 1)

hypertension & is defined by a blood pressure over 140 mmHg systolic or 90 mmHg diastolic & less than 159 mmHg systolic or 99 mmHg. The third classification of hypertension is (stage 2) hypertension & defined by blood pressure over ≥ 160 mm Hg or diastolic ≥ 100 mm Hg (JNCVII) [1]. It affects approximately one-third of the world's adult population and it is predicted to increase with 60% towards 2025[2]. It is also associated with a number of serious conditions and accounts for instead of 13.5% of all premature deaths, 54% of all strokes and 47% of ischemic heart diseases.[3] Hypertension is the most common root of cardiovascular disorder which has become a global problem with worldwide prevalence and increases with advancing age; for example, about 50% of people between the ages of 60 and 69 years old have hypertension, and the prevalence is further increased beyond age 70[4]. Important risk factor for coronary artery disease, stroke, renal failure and peripheral vascular disease. Beta-blockers presently, preferred in treatment for hypertension. Nebivolol is a selective β_1 -blocker and lipophilic in nature it also has nitric oxide potentiating vasodilator effect. [5-8] Atenolol is a hydrophobic β_1 blocker.

MATERIAL & METHODS:

A comparative, prospective, open label, parallel group study of 12 weeks was conducted by the Department of Pharmacology in association with Department of Medicine in patients of Stage 1 hypertension from Jan 2011 to June 2012 at MMIMSR, Mullana, Ambala. The research protocol was approved by the Institutional Ethics Committee. Sixty patients of both the sexes within the age group 18 to 70 years after fulfilling the

inclusion and exclusion criteria were enrolled and were divided into 2 groups. Group A patients received Atenolol 50 mg oral once a day for 12 weeks and Group B patients received Nebivolol 5mg oral once a day for 12 weeks. Patients with history of drug allergy, alcohol intake, bronchial asthma, chronic obstructive pulmonary disease (COPD), congestive cardiac failure, coronary artery disease, diabetes mellitus, peripheral arterial disease and female patients who were pregnant, lactating or not employing adequate measures to prevent conception were excluded. All the patients gave their written consent before enrolment in the study. Clinical evaluation of all the patients was done by measuring blood pressure and heart rate before administration of drug. Follow up was done at 2, 4, 8 and 12 weeks. Safety or tolerability evaluation was based upon both self reported adverse effects and the recorded adverse effects. Data were collected and the analyzed by using Student's t test (paired and unpaired). Statistical significance was defined as $p < 0.05$ and highly significant was defined as $p < 0.001$.

RESULTS:

Sixty patients were included in the study, of which 30 received Nebivolol 5mg once daily and the other 30 patients received Atenolol 50mg once daily. All the patients completed the study depicts the demographic data of the patients. In the Nebivolol group 60% were males and 40% with their mean age being 48.1 ± 13.5 years. Among the patients who received Atenolol 50% were males 50% females with the mean age group of 40.4 ± 10.8 years. There was no statistically significant difference between the ages of patients between the patients of two groups. (Table 1)

	Atenolol Group	Nebivolol Group	p – value
Age (mean \pm sd)	40.4 \pm 10.8	48.1 \pm 13.5	> 0.05
Male/Female (%)	15/15 (50/50)	18/12 (60/40)	> 0.05

The mean heart rate reduced from 86.8 ± 1.9 beats/min to 78.9 ± 1.5 beats/min from baseline to 12 weeks in group A ($p < 0.001$). The mean heart rate reduced from 85.5 ± 2.0 beats/min to 75.1 ± 2.5 beats/min from baseline to 12 weeks in group B ($p < 0.001$). There was statistically significant reduction in heart rate observed with both treatment groups. (Table 2)

Drugs	At Baseline Mean \pm SD	At 12 weeks Mean \pm SD	p -value
Atenolol	86.8 \pm 1.9	78.9 \pm 1.5	< 0.001
Nebivolol	85.5 \pm 2.0	75.1 \pm 2.5	< 0.001

Mean SBP was reduced from 150.07 ± 6.84 mm Hg to 130.87 ± 2.72 mm Hg (Atenolol) and 153.27 ± 5.99 mm Hg to 128.40 ± 4.36 mm Hg (Nebivolol) after 12 weeks treatment (percentage difference was 12.79%, 16.22%). Both drug decrease systolic blood pressure from baseline to after treatment of 12 week which is statically highly significant (Table 3 Figure 1).

Table 3: Assessment of antihypertensive effect of Atenolol and Nebivolol in the reduction of SBP

	Atenolol Group		Nebivolol Group	
	Mean ± SD	p-value	Mean ± SD	p-value
Baseline	150.07 ± 6.84		153.27 ± 5.99	
Week 2	145.27 ± 3.17	< 0.001	149.07 ± 5.74	< 0.001
Week 4	140.40 ± 5.10	< 0.001	142.20 ± 5.85	< 0.001
Week 8	134.73 ± 2.99	< 0.001	134.27 ± 5.11	< 0.001
Week 12	130.87 ± 2.72	< 0.001	128.40 ± 4.36	< 0.001

Mean DBP was reduced from 93.00 ± 3.17 mm Hg to 80.33 ± 2.37 mm Hg (Atenolol) and 94.88± 2.57 mm Hg to 80.00 ± 2.58 mm Hg (Nebivolol) after 12 weeks treatment (percentage difference was 13.62%, 15.68%). Both drug decrease diastolic blood pressure from baseline to after treatment of 12 week which is statically highly significant (Table 4 Figure 2).

Table 4: Assessment of antihypertensive effect of Atenolol and Nebivolol in the reduction of DBP

	Atenolol Group		Nebivolol Group	
	Mean ± SD	p-value	Mean ± SD	p-value
Baseline	93.00 ± 3.17		94.88± 2.57	
Week 2	90.27 ± 2.52	< 0.001	92.47 ± 2.17	< 0.001
Week 4	86.53 ± 2.12	< 0.001	88.47 ± 1.84	< 0.001
Week 8	83.20 ± 1.83	< 0.001	85.20 ± 2.04	< 0.001
Week 12	80.33 ± 2.37	< 0.001	80.00 ± 2.58	< 0.001

Figure 1: Bar Chart Comparison of efficacy in SBP reduction by both the groups.

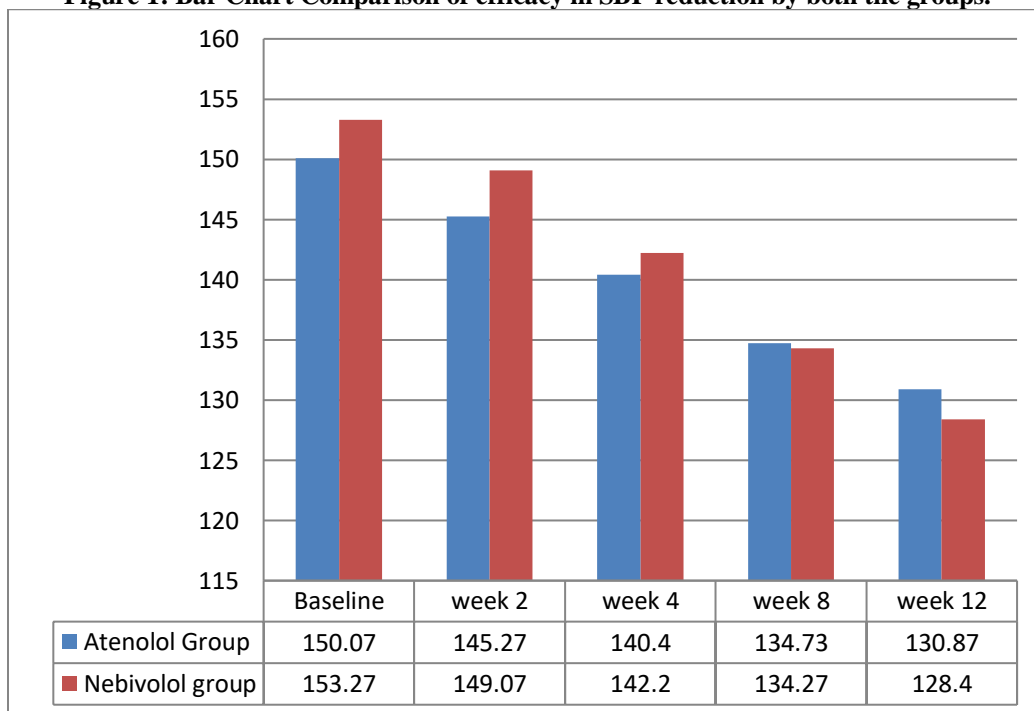
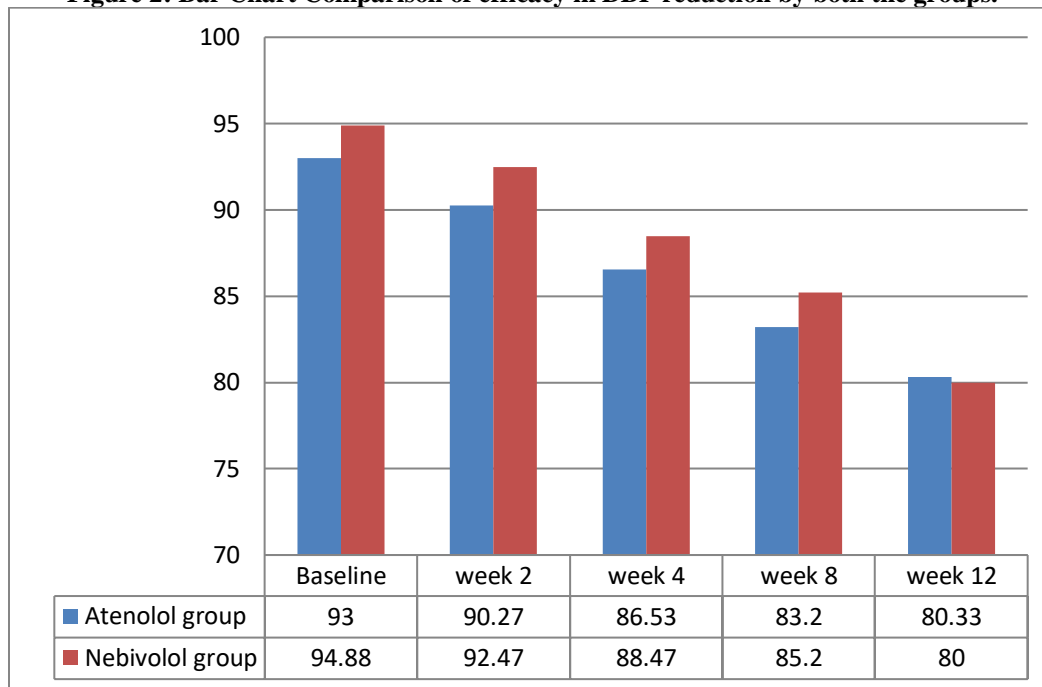


Figure 2: Bar Chart Comparison of efficacy in DBP reduction by both the groups.

We also compared the reduced mean SBP and DBP from baseline to 12 weeks between both groups (inter group analysis of Atenolol and Nebivolol) which is not statistically significant ($p > 0.05$) (Table 5).

A total of 01 (3.3%) patients experienced adverse drug reactions in group A and 03 (10%) in group B; all were mild and did not require any alteration or discontinuation of treatment. 01 (3.3%) subjects reported headache in group A. 01 (3.3%) subject reported dizziness, 01 (3.3%) subject reported nausea, and 01 (3.3%) subject reported fatigue in group B.

Table 5: Comparison between Atenolol group and Nebivolol group of Systolic and Diastolic Blood Pressure

	Atenolol Group	Nebivolol Group		Atenolol Group	Nebivolol Group	
	SBP	SBP	p-value	DBP	DBP	p-value
	Mean \pm SD	Mean \pm SD		Mean \pm SD	Mean \pm SD	
Baseline	150.07 \pm 6.84	153.27 \pm 5.99	> 0.05	93.00 \pm 3.17	94.88 \pm 2.57	> 0.05
Week 2	145.27 \pm 3.17	149.07 \pm 5.74	> 0.05	90.27 \pm 2.52	92.47 \pm 2.17	> 0.05
Week 4	140.40 \pm 5.10	142.20 \pm 5.85	> 0.05	86.53 \pm 2.12	88.47 \pm 1.84	> 0.05
Week 8	134.73 \pm 2.99	134.27 \pm 5.11	> 0.05	83.20 \pm 1.83	85.20 \pm 2.04	> 0.05
Week 12	130.87 \pm 2.72	128.40 \pm 4.36	> 0.05	80.33 \pm 2.37	80.00 \pm 2.58	> 0.05

DISCUSSION:

This study was done to compare the efficacy and safety of atenolol and nebivolol in the management of hypertensive patients attending a tertiary care teaching hospital.

The mean heart rate reduced from 86.8 ± 1.9 beats/min to 78.9 ± 1.5 beats/min from baseline to 12 weeks in group A ($p < 0.001$). The mean heart rate reduced from 85.5 ± 2.0 beats/min to 75.1 ± 2.5 beats/min from baseline to 12 weeks in group B ($p < 0.001$). The results of this study showed that both atenolol and nebivolol

significantly reduced mean heart rate from baseline to 12 weeks ($p < 0.001$).

A similar study conducted by Swathi Ropale has shown the same results after treatment of 12 weeks. [9]

The primary endpoint of the study was the change in mean systolic blood pressure (SBP) & (DBP) from baseline to 12 weeks. The results of this study showed that both atenolol and nebivolol significantly reduced mean SBP & DBP from baseline to 12 weeks ($p < 0.001$).

We also compared the reduced mean SBP and DBP from baseline to 12 weeks between both groups (atenolol and nebivolol) which is not statistically significant ($p > 0.05$) (Table 5). Thus, concluding that, although both atenolol and nebivolol produced statistically significant reduction in SBP as well as DBP, there is no difference between the treatment groups. They are both equally efficacious in the treatment of HTN. Our findings are consistent with previous studies that have shown that both atenolol and nebivolol are effective in reducing blood pressure in hypertensive patients.

A study showed the reduction in SBP in nebivolol group was 151.53 ± 10.4 mm of Hg to 134.25 ± 4.6 mm of Hg. And in atenolol group it was from 153.63 ± 8.4 mm of Hg to 136.73 ± 6.08 mm of Hg after three months. The reduction in DBP in nebivolol group was from 97.53 ± 2.4 mm of Hg to 86.76 ± 2.64 mm of Hg. And in atenolol group it was from 97.89 ± 3.47 mm of Hg to 87.84 ± 4.06 mm of Hg after three months.

This study shown that both the drugs had significant anti hypertensive effect. [10]

A similar study for three months in which they showed that both atenolol and nebivolol had significant anti hypertensive effect but when compared there is no statistical significance between the two drugs ($p > 0.001$). The reduction in SBP in nebivolol group was from 158 ± 17 mm of Hg to 118 ± 8 mm of Hg and in atenolol group was from 160 ± 16 mm of Hg to 115 ± 7 mm of Hg after three months. The reduction in DBP in nebivolol was from 97 ± 10 mm of Hg to 71 ± 3 mm of Hg and in atenolol group was from 99 ± 10 mm of Hg to 71 ± 3 . The present study also proves that there is no statistical significance in the anti hypertensive effect of the two drugs at the end of three months. [11]

A multicentre study showed the efficacy of atenolol and nebivolol are compared in mild and moderate hypertensive patients. The study was conducted for three months. The study supports our study by saying that the two drugs show significant anti hypertensive effect at the end of three months. The reduction in SBP and DBP was 18.12 ± 14.10 mm of Hg and 14.6 ± 7.9 mm of Hg in atenolol group. And it was 19.1 ± 12.9 mm of Hg and 14.8 ± 7.1 mm of Hg for nebivolol group. [12]

A study conducted by Porrier et al., has shown the similar anti hypertensive effects of atenolol and nebivolol. [13]

In addition to blood pressure reduction, our study also evaluated the safety of atenolol and nebivolol. The results showed that both drugs were well-tolerated, with no serious adverse events reported in either group. The adverse effects reported were nausea, fatigue, dizziness and headache, which are known side effects of both drugs.

Limitations of this study are it is an open-labeled study. Only 12-week follow-up is not sufficient.

CONCLUSION:

The study showed that both Atenolol and Nebivolol are equally effective in reducing systolic and diastolic blood pressure and heart rate.

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