

“A comparative study of Nebivolol plus Amlodipine and Atenolol plus Amlodipine on blood pressure and heart rate in patients of essential hypertensive patients”

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Abstract

Objectives: Study was conducted to compare the evaluation of efficacy and safety of Nebivolol plus Amlodipine combination with Atenolol plus Amlodipine combination in hypertensive patients.

Materials and Methods: A Prospective Observational study was conducted at tertiary care teaching hospital which included a total 334 patients with essential hypertension. The demographic and baseline data, Blood pressure and Heart rate of the patients were recorded. After baseline investigation patients were randomly divide into 2 groups. All patients were subsequently monitored and reassessed at 4th-week, 8th week and 12th weeks of interval during each follow-up.

Results: Nebivolol plus Amlodipine group include a total 169 patients in which 129 patients were males and 40 patients were females with mean age 46.89 ± 12.48 years, Atenolol plus Amlodipine group include a total 165 patients in which 111 patients were males and 54 patients were females with mean age 48.19 ± 12.14 years. Patients were receiving Nebivolol plus Amlodipine and Atenolol plus Amlodipine showed a significant fall in systolic blood pressure (SBP), Diastolic blood pressure (DBP) and Heart rate at the end of 4th, 8th and 12th weeks of interval as compared to their baseline data.

Conclusion: A Study reveals that Reduction of blood pressure and Heart rate were similar in both treatment groups (Nebivolol plus Amlodipine and Atenolol plus Amlodipine). (P- value >0.05)

Keywords: hypertensive patients, Nebivolol plus Amlodipine, Atenolol plus Amlodipine.

INTRODUCTION

According to WHO 25 August 2021 Hypertension or high blood pressure associated with serious medical condition that increases the risks of heart, brain, kidney and other diseases. About 1.28 billion adults aged 30-79 years worldwide have increase blood pressure among them most (two-thirds) living in low- and middle- socioeconomic status countries. about 46% of adults with hypertension are unaware that they have the condition. Less than half of adults (42%) with hypertension are diagnosed and treated. Approximately 1 in 5 adults (21%) with hypertension have it under control. It is major cause of premature death worldwide.

High blood pressure is the third most important risk factor for attributable burden of the disease in south Asia¹. As per WHO Global Health Observatory Data 2008 high blood pressure directly responsible for 57% of all stroke deaths and 24% of all coronary heart disease deaths in India².

According to the WHO 2008 estimates, the prevalence rate of high blood pressure in Indians was 32.5% (33.2% in men and 31.7% in women)³. However, only about 25.6% of treated patients had their BP under control, in a multi-centred study from India on awareness, treatment, and adequacy of control of Hypertension⁴.

Now Various treatment option available for the treatment for the essential hypertension, beta blockers are one of the effective drugs for primary and secondary prevention of coronary artery disease among them Nebivolol is a third-generation cardio-selective beta blocker which reduced blood pressure by beta 1 blockade and vasodilation by stimulation of nitric oxide release, which leads to vasodilation and is associated with reduction in peripheral vascular resistance⁵. Due to this dual mechanism of action it is supposed to exert a better control of blood pressure ⁶. For the same reason tolerability profile of Nebivolol is hypothesized to be favourable compared to other beta blockers in hypertensive patients and has positive effect on general well-being so that it preserves quality of life⁷. others Available beta blocker like Atenolol is also one of the most widely used in patients of essential hypertension. Hence, in present study Nebivolol plus Amlodipine is used to compare the efficacy and safety of anti-hypertensive Atenolol plus Amlodipine.

MATERIAL AND METHODS

Study Design and Site

This was a Comparative, Prospective and Observational study which was conducted in Department of Pharmacology at Santosh Medical College and Hospital Ghaziabad in collaboration with and FH Medical College and Hospital Agra, Utter Pradesh entitled “A comparative study of Nebivolol plus Amlodipine and Atenolol plus Amlodipine on blood pressure and heart rate in patients of essential hypertensive patients”

Study population

Total 334 Newly - diagnosed Patients of Hypertension (Age 18 – 80 yrs of either sex) From Medicine OPD Of F.H. Medical College and hospital.

Methodology

After initial screening among the patients, their socio-demographic data regarding Age, Sex, Education status, Socioeconomic status etc will be recorded in a case form. Blood pressure, Heart Rate, of patients estimated at baseline. After baseline investigation patients will be randomly divide into 2 groups.

- Nebivolol group which receive Nebivolol 5 mg plus Amlodipine 5 mg OD.
- Atenolol group was receive Atenolol 25 mg plus Amlodipine 5 mg OD.

Patients under the study will be subsequently monitored and reassessed at 4-week, 8 week and 12 weeks, during each follow-up.

Statistical Analysis - Frequency and percentages have been used to represent categorical variable. Mean and Standard variation has been used to represent the continuous variables. For intra group comparison repeated measures ANOVA has used, while for between group comparison independent t test has used. The data were analyzed using SPSS Software (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 28.0. Armonk, NY: IBM Corp.). A two-tailed p-value less than 0.05 was defined as statistical significance

Result and Observations:- Total 334 patients were included in the study, of which 169 Received Nebivolol 5 mg plus Amlodipine 5 mg once daily and the other 165 patients received Atenolol 25 mg plus Amlodipine 5 mg once daily. Participants who completed all the information were taken.

Table 1- Demographic data of the patients who received Nebivolol 5 mg plus Amlodipine 5 mg once daily, 76.3 % were Male and 23.7 % female with their mean age being 46.89 ± 12.48 years. In this group 63.3 % participant were reside in rural area,

76.3 % were married, only 59.8 % were literate, 74 % of respondents were poor by socioeconomic status. 59.2 % were smoker. Among the patients who received Atenolol 25 mg plus Amlodipine 5 mg once daily 67.3% were males and 32.7 % females with mean age 48.19±12.14. About 70% participants reside in rural area, 79.4% were married. Around 72 % were literate, most of them belongs to poor family by socioeconomic class. More than half were smoker.

Table 1- Demographic characteristics of Nebivolol and Atenolol group

Particulars of the patients	Nebivolol	Atenolol
Number	169	165
Age(Mean ±SD)	46.89 ±12.48	48.19±12.14
Gender		
Male	129(76.3)	111(67.3)
Female	40(23.7)	54(32.7)
Residence		
Urban	62(36.7)	49(29.7)
Rural	107(63.3)	116(70.3)
Marital status		
Unmarried/ Divorced/ Separated	40(23.7)	34(20.6)
Married	129(76.3)	131(79.4)
Education level		
Illiterate	68(40.2)	46(27.9)
Literate	101(59.8)	119(72.1)
Socio-economic status		
Poor	125(74.0)	111(67.3)
Good	44(26.0)	54(32.7)
Smoking		
Yes	100(59.2)	95(57.6)
No	69(40.8)	70(42.4)

Table 2- Show the effect of Atenolol produced highly significant reduction in both systolic and diastolic blood pressures. Systolic blood pressure at the baseline was 159.41 ± 10.98 mmHg was reduced to 151.15 ± 11.33, 131.31 ± 11.99, 128.27 ± 9.37 mmHg at the end of 4th, 8th, and 12th week of treatment, respectively, (p-value <0.0001). and Diastolic blood pressure was decreased from 99.50± 6.15 mmHg to 92.59±7.14, 86.72±7.43, 80.55±4.40 mmHg at the end 12 week which is highly significant. (p-value <0.0001).

Table 2- Effect Atenolol on blood pressure

S.No.	Parameter	Atenolol	
		S.B.P	D.B.P
1	Baseline	159.41±10.98	99.50±6.15

2	After 4 week	151.16±11.31	92.59±7.14
3	After 8 week	131.31±11.99	86.72±7.43
4	After 12 week	128.27±9.37	80.55±4.40
5	p-value	<0.0001	<0.0001

Table 3- Show the effect of Nebivolol produced highly significant reduction in both systolic and diastolic blood pressures. Systolic blood pressure at the baseline was 159.59±11 mmHg was reduced to 149.48±11.18, 124.44±15.22, 116.05±14.03 mmHg at the end of 4th, 8th, and 12th week of treatment,(P value <0.0001). Diastolic blood pressure was decreased from 99.48±5.54 mmHg to 89.25±6.42, 79.85±5.05, 77.62±5.18 mmHg at the end 12 week which is highly significant (P-value <0.0001).

Table 3- Effect of Nebivolol on blood pressure

S.No.	Parameter	Nebivolol	
		S.B.P	D.B.P
1	Baseline	159.59±11	99.48±5.54
2	After 4 week	149.48±11.18	89.25±6.42
3	After 8 week	124.44±15.22	79.85±5.05
4	After 12 week	116.05±14.03	77.62±5.18
5	p-value	<0.0001	<0.0001

Table 4- Both drug Nebivolol and Atenolol produced significant reduction in systolic blood pressure in from baseline, On intra group comparison reduction in systolic blood pressure was slightly higher with Nebivolol as compared to Atenolol, the result was not statically significant after 4th week (P 0.081), 8th week (P 0.241) and after 12th week of treatment (P 0.7581)

Table 4- Compare Effect of Nebivolol & Atenolol on systolic blood pressure

S.No.	Parameter	Atenolol	Nebivolol	p-value
		S.B.P	S.B.P	
1	Baseline	159.41±10.98	159.59±11	0.880
2	After 4 week	151.16±11.31	149.48±11.18	0.081
3	After 8 week	131.31±11.99	124.44±15.22	0.241
4	After 12 week	128.27±9.37	116.05±14.03	0.7581
5	P- Value	<0.0001	<0.0001	

Table 5- Both drug decrease diastolic blood pressure from baseline to after treatment of 12 week which is statically highly significant, On other hand intra group comparison the reduction diastolic blood pressure was slightly higher with Nebivolol as compared to Atenolol, the result was not statically significant after 4th week (P 0.081), 8th week (P 0.154) and after 12th week of treatment (P 0.458).

Table 5- Compare Effect of Nebivolol & Atenolol on diastolic blood pressure

S.No.	Parameter	Atenolol	Nebivolol	p-value
		D.B.P	D.B.P	
1	Baseline	99.50±6.15	99.48±5.54	0.975
2	After 4 week	92.59±7.14	89.25±6.42	0.081
3	After 8 week	86.72±7.43	79.85±5.05	0.154
4	After 12 week	80.55±4.40	77.62±5.18	0.458
5	P-Value	<0.0001	<0.0001	

Table 6- Show the effect of Nebivolol on Heart rate which was reduced significantly from 90.47±3.34 to 88.11±4.48, 83.18±4.71, 79.84 ± 3.78 at the end of 4th, 8th, and 12th week, (P <0.0001). while there was significant (p<0.0001) gross reduction in heart rate from 90.38±3.45 to 87.92±4.50, 82.68±4.69, 78.65±3.56 at the end 4th, 8th, and 12th week as compared to the baseline of Atenolol. On intra group comparison reduction of Heart rate slightly higher with Atenolol at 12th week as compared to Nebivolol which result was significant (P- value 0.003)

Table 6- Compare the Effect of Nebivolol & Atenolol on Heart Rate

Parameters	Heart Rate		
	Atenolol	Nebivolol	p-value
Baseline	90.38±3.45	90.47±3.34	0.807
After 4 week	87.92±4.50	88.11±4.48	0.696
After 8 week	82.68±4.69	83.18±4.71	0.327
After 12 week	78.65±3.56	79.84±3.78	0.003
p-value	<0.0001	<0.0001	

Discussion

The newer hypertension treatment guidelines from National Institute for Health and Clinical Excellence (NICE) and the British Hypertension Society (BHS) recommend that “β blockers should no longer be used as first-line drugs for the treatment of uncomplicated hypertension.” This recommendation is based on the evidence of various studies of Atenolol alone or in addition diuretics increases the risk of new onset diabetes mellitus than other medicines such as ACE inhibitors, angiotensin receptor blockers and calcium channel blockers, due to its adverse effect on carbohydrate and lipid metabolism. Hence, β-blockers are now reserved as third- or fourth-line medicines⁸. Patients treated with atenolol (±diuretics) have 30% higher chances of new onset diabetes compared to those receiving calcium channel blockers (±ACE inhibitors)⁹.

In our study, we have compared the evaluation of efficacy and safety of Nebivolol plus Amlodipine combination Between Atenolol plus Amlodipine combination in hypertensive patients. Literature search has revealed comparison of effect of nebivolol once daily with racemic mixture of atenolol once daily on blood pressure, heart rate, and oxidative stress in essential hypertensive patients¹⁰⁻¹¹. Studies comparing nebivolol (S)-atenolol were less in number, hence this study was carried out.

In our study, we have observed a significant reduction of SBP and DBP in patients who received Nebivolol plus Amlodipine combination. Between Atenolol plus Amlodipine combination in hypertensive. The effect was observed at the end of 4th, 8th and 12th weeks of treatment from the baseline data which is similar to studies conducted by Van Nueten et al¹². However drug Nebivolol plus Amlodipine produced more reduction in systolic and diastolic blood pressure as compared to Atenolol plus Amlodipine which not significant. Which is similar to study conducted by G.N. Sahana et al¹³.

Our study also find that significant reduction in the heart rate after 12 weeks from baseline with both drugs but more slightly more reduction in heart rate with Atenolol plus Amlodipine as compared to Nebivolol plus Amlodipine which was observed in previous studies¹⁴⁻¹⁷.

Being sympatholytic, nebivolol decreases sympathetic activity and the vasodilator property may reflexly accelerate the parasympathetic activity. It has been observed that nebivolol attenuates the sympathetic tone, but does not promote vagal activity more than atenolol. Hence, fall in the heart rate with nebivolol is slightly less as compared to atenolol¹⁸.

Conclusion:

In intra group comparison reduction of blood pressure (systolic and diastolic) and Heart rate with Nebivolol plus Amlodipine and Atenolol plus Amlodipine was similar, however reduction blood pressure and Heart rate after 12th week from baseline to was highly significant in both treatment groups.

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