Original Article

Comparison of Effectiveness Between Nebivolol and Bisoprolol in Treating Hypertensive Patients

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Abstract:

Hypertension is the leading cause of cardiovascular disease. Beta blockers are prescribed for hypertension, heart failure, angina pectoris or a history of myocardial infarction. In this study, we have compared the effectiveness between two beta blockers, i.e. Nebivolol and Bisoprolol in hypertensive patient.

A randomized prospective study was conducted from 1st January to 31st July 2022 at Jashore Medical College Hospital, Jashore in the outpatient department of medicine after maintaining all ethical issues. Five hundred twenty eight hypertensive patients without other comorbidities were studied after informed written consent. Patients were followed up for three months.

Out of 528 patients 264 were received Nebivolol. In this case group 40 patients were missed in follow up. And among 224 patients, 198 patients were found optimum reduction of blood pressure which was 88.39% out of 224. Rest 264 were received Bisoprolol. In this case group 58 patients were missed in follow up. And among 206 patients, 176 patients were found optimum reduction of blood pressure which was 85.43% out of 206.

In this study Nebivolol showed superiority in reduction of blood pressure in comparison to Bisoprolol that is 2.95%. Large sc ale trials along with comorbidities, mortality and hospital stay reduction as well as strict follow up are needed to compare various beta blockers.

Keywords: Beta blockers, Bisoprolol, Nebivolol

Introduction:

Beta blockers differ with respect to their mechanisms of action, especially in terms of beta-1 adrenoceptor selectivity and vasoactive effects[1]. First generation beta blockers are non-cardio selective (Propranolol) whereas second generation beta blockers are more beta-1 selective (e.g. Metoprolol, Atenolol etc). Third generation agents have not only beta adrenoceptor blocking properties but also vasodilating properties (e.g. Carvedilol, labetalol, nebivolol)[2-3]. Beta blockers are choice of drug in controlling hypertension, angina, heart failure and ischaemic heart disease. Many data explained that nebivolol has some special effects on endothelial dysfunction, aortic stiffening and central venous pressure. Nebivolol shows no significant increase risk on new onset diabetes mellitus as compare to other beta blockers[4]. In Bangladesh these two drugs have been used for a decade but there is no suitable data in comparison to their effectiveness. So, this study showed their effectiveness in controlling hypertension.

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Received Date : 10 November, 2023

Accepted Date : 15 November, 2022

Materials and methods:

This randomized prospective study was conducted from 1st January 2022 to 31st July 2022 at Jashore Medical College Hospital, Jashore. Five hundred twenty-eight (528) participants were studied after informed written consent. Group-A was given Nebivolol and group-B was given Bisoprolol. Patients age, gender, smoking, family history and duration of hypertension were noted in self structured questionnaire. Their blood pressures were measured in outdoor medicine department and follow up were counted in every month up to 3 months. All collected data were analyzed by using SPSS (Statistical Packagefor Social Science) version-22. Frequency and

The Journal of Ad-din Women's Medical College; Vol. 11 (1), Jan 2023; p 33-37
https://doi.org/10.3329/jawmc.v11i1.70466

percentage for categorical variables, *M(±SD)* and Chi-square test were used among categorical variable to determine the association between outcome and independent variables. A *p* value less than .05 were considered as significant all through.

Ethical Approval:

Ethical clearance was obtained from the Ethical Review Committee (ERC) and Institutional Review Board (IRB) of Ad-din Sakina Women's Medical College (ASWMC), Jashore.

Results:

Out of 528 patients 264 received nebivolol. Of which 40 patients dropped out of were missed in following up. In this group of 224 patients, 198 had optimum reduction of blood pressure (88.39%). Of 264 were receiving Bisoprolol, 58 were missed in follow up. Thus 206 patients, 176 patients had an optimum reduction of blood pressure.

This findings demonstrates that study nebivolol showed superiority in reduction of blood pressure by 2.9% in comparison to that of Bisoprolol had.

Table I

Association between age groups and genders of patients (n = 528)

Age Group	Gender		Statistical Association, P-value
	Female (n=289)	Male (n=239)	
25-45 years(n=90)	56	34	χ^2=4.97
46-65 years(n=365)	188	177	P-value=.08,
66-85 years(n=73)	45	28	df=2

Majority of the respondents both male and female belong to the age group of 46-65 years. Here the statistical association between age groups and gender was not found significant (P=0.08) (Table I).

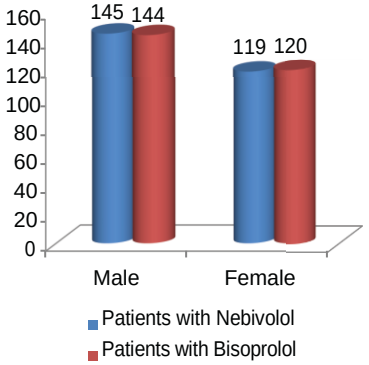

Table 2: *Gender specific distribution of hypertensive patients receiving Nebivolol and Bisoprolol of the patients (n=528)*

Out of total 528 patients, 264 received Nebivolol and majority (145 respondents) in this case group were men. The remaining 264 patients received bisoprolol, with majority of 144 male patients.

Table-II

Association between age groups and family history of patients

Age Group	Family history		Statistical Association, P-value
	Yes (n=27)	No (n=501)	
25-45 years(n=90)	3	87	χ^2=0.70
46-65 years(n=365)	20	345	P-value=0.70
66-85 years(n=73)	4	69	df=2

The majority of patients, from (46-65) years, reported no history of hypertension in their families which was not statistically significant (P=0.70).

Table III

Age of the patients (n=528)

Age of the patients	Patients with Nebivolol (n=264)	atients with PBisoprolol (n=264)
(Mean±SD)	54±9	55±9
25-45years	51 (19%)	39 (15%)
46-65 years	176 (66%)	189 (72%)
66-85 years	37 (14%)	36 (14%)

Mean age of patients with Nebivolol and Bisoprolol were (54±9) and (55±9) respectively. Patients aged (46-65) years make up 66% of Nebivolol patients and 72% of Bisoprolol patients.

Table IV

Distribution of Antihypertensive Drug (n=528)

Blood Pressure (mmHg)	Patients with Nebivolol (n=264)	Patients with Bisoprolol (n=264)	P-value
Systolic blood pressure, mmHg	145±7	146±7	0.47
Diastolic blood pressure, mmHg	90±2	91±2	0.83

In comparison between Nebivolol and Bisoprolol patient's Systolic (P=0.47) and Diastolic blood (P=0.83) pressure, there had no difference.

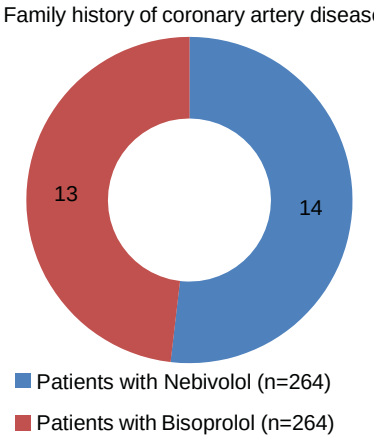

Figure-2: *Family history of coronary artery disease (n=528)*

Family history of coronary artery disease had been identified in 14 and 13 patients, respectively, out of 264 patients using nebivolol and bisoprolol.

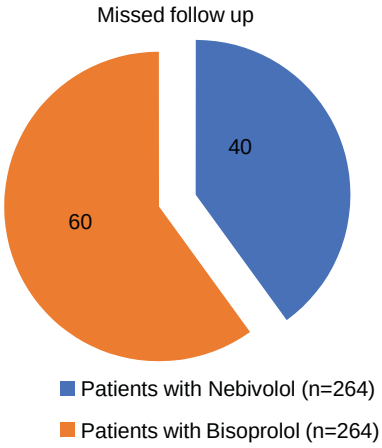

Figure-3: *Missed patients during follow up (n=528)*

The number of patients missed during follow-up among those using nebivolol and bisoprolol was 60 and 40, respectively.

Table-V

Association between age groups and drugs

Age Group	Drugs		Statistical
	Nebivolol (n=264)	Bisoprolol (n=264)	Association P-value
25-45 years(n=90)	51	39	χ^2=2.07
46-65 years(n=365)	176	189	P-value=0.35
66-85 years(n=73)	37	36	df=2

In both cases integrating nebivolol and bisoprolol, the majority of patients were found to be between the ages of (46 - 65) years and no statistical significance was found (P= 0.35).

Table-VI

Association between gender and drugs

Age Group	Drugs		Statistical
	Nebivolol (n=264)	Bisoprolol (n=264)	Association, P-value
Male (n=289)	145	144	χ^2=0.08
Female (n=239)	119	120	P-value=0.93, df=1

Male patients accounted for a larger proportion of those using Nebivolol and Bisoprolol than female patients and gender and drugs were not statistically not associated (P=0.93).

Table-VII

Association between drugs and missing patient

Drugs	Follow up		Statistical
	Missed (n=100)	Follow up (n=428)	Association, P-value
Nebivolol (n=264)	40	224	χ^2=1.35
Bisoprolol (n=264)	60	204	P-value=0.02, df=1

In Nebivolol and Bisoprolol case group 40 and 60 patients respectively were missed in follow up (P=0.02).

Table VIII

Comparison between Nebivolol and Bisoprolol patient's Systolic blood pressure (mmHg) (n=528)

	Systolic blood pressure, mmHg before medicated	After Systolic blood pressure, mmHg after medicated	P-value
Nebivolol	144±7	122±4	<0.001
Bisoprolol	144±7	143±7	0.23

In comparison between Nebivolol and Bisoprolol patient's Systolic blood pressure, Nebivolol case was more significant (P<0.001) than Bisoprolol case (P=0.23)

Table IX

Comparison between Nebivolol and Bisoprolol patient's Diastolic blood

	Diastolic blood pressure, mmHg before medicated	Diastolic blood pressure, mmHg after medicated	p-value
Nebivolol	90±2	82 4	<0.001
Bisoprolol	91±2	90 4	0.33

In comparison between Nebivolol and Bisoprolol patient's Diastolic blood pressure, Nebivolol case was more significant (P<0.001), than Bisoprolol case (P=0.33)

Discussion:

Hypertension is a globally reported risk factor developing ischemic heart disease (IHD), heart failure, stroke, atrial fibrillation, peripheral vascular disease etc. Blockers remains the first-line treatment against hypertension reported to be beneficial in primary and secondary prevention of coronary artery disease (CAD).[5, 6] Nebivolol, a third-generation (profoundly) β1-selective blocker is primarily been utilized for mild and moderate essential hypertension or combined with standard therapeutic drugs as some studies yielded. [5, 7-8]

Nebivolol and bisoprolol are highly selective β 1-adrenoceptor antagonists having clinical indications in many countries for the treatment of heart failure with reduced left ventricular ejection fraction (HFrEF), ischemic heart disease (IHD), and hypertension.[9]

Nebivolol and bisoprolol had similar impact on the mean change of diastolic blood pressure (DBP) and systolic blood pressure (SBP), according to a previous study, showing no difference in the overall incidence of AEs. Findings of a meta-analysis reported that nebivolol, compared to other blockers had no discernible difference with other second-generation β blockers in reducing blood pressure, SBP, and DBP.[10]

Findings of this study showed a clear-cut superiority of nebivolol over bisoprolol in reducing/ controlling blood pressure. Another study on bisoprolol showed that it reduces cardiovascular events too. [10] While a different study showed that nebivolol reduces mortality and cardiovascular hospitalization compared to that of placebo.[11, 12]

Due to super selectivity and unique mechanisms of nebivolol it protects more CVD cases since it has greater affinity on human cardiac beta-1 than beta-2 receptors, being more selective.[13] Nebivolol is 3.5 times more beta -1 adrenoceptor selective than that of bisoprolol and nebivolol not only decrease nitric oxide (NO) but also inhibits proliferation of human coronary endothelial cells and aortic smooth muscle cells via NO delivery. [14, 15]

This study therefore evidence that nebivolol remains superior to that of bisoprolol, but needs to be follow up uses of β- blockers, strictly.

Conclusion:

Our findings attest that, nebivolol and bisoprolol remains quite good in controlling of hypertension irrespective of patients' age and sex. In comparison to bisoprolol, nebivolol showed superiority in reduction of blood pressure by 2.95%. However, large scale clinical trials are needed to be conducted on the comparison of nebivolol and bisoprolol involving comorbidity, mortality, hospital stay including other beta blockers specially these two (nebivolol and bisoprolol).

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