

**THE CLINICAL OUTCOME OF IVABRADINE AND NEBIVOLOL IN THE
TREATMENT OF STABLE ANGINA PECTORIS PATIENTS WITH MILD LEFT
VENTRICULAR DYSFUNCTION****Dr. Mohammad Rashedul Hasan*¹ and Dr. Mahmudul Hasan²**¹Senior Consultant, Dept. of Cardiology, Noakhali 250- Bed General Hospital, Noakhali, Bangladesh.²Junior Consultant, Dept. of Cardiology, Noakhali 250- Bed General Hospital, Noakhali, Bangladesh.***Corresponding Author: Dr. Mohammad Rashedul Hasan**

Senior Consultant, Dept. of Cardiology, Noakhali 250- Bed General Hospital, Noakhali, Bangladesh.

Article Received on 10/01/2021

Article Revised on 31/01/2021

Article Accepted on 21/02/2021

ABSTRACT**Background:** In chronic stable angina, increased heart rate contributes to the development of symptoms and signs of myocardial ischaemia by increasing myocardial oxygen demand and reducing diastolic perfusion time.**Objective:** In this study our main goal is to evaluate the clinical outcome of Ivabradine and Nebivolol in the Treatment of Stable Angina Pectoris Patients with Mild Left Ventricular Dysfunction. **Methods:** This cross-sectional observational study was done at Noakhali 250-Bed General Hospital from April 2020 to December 2020. A total of 200 consecutive patients were included. The patients were evaluated in 2 different groups (1,2). In group-1 Nebivolol 5mg/day was administered to the 100 patients included in Group A. 100 patients were started on Ivabradine 10mg/day and these patients were included into group-2. **Result:** During the study, according to systolic Diastolic BP and heart rate heart rate decreased (79 ± 7) to (66 ± 5.1) in Group: 1 and (78 ± 7) to (71 ± 5) in Group: 2. After 6 months' treatment LVEF for the group-1 improved by (45 ± 6.5) to (52 ± 3.1), and for the group-2 (48 ± 5.5) to (53 ± 2.1). There is no significant change in EF improvement in both groups. Also, dose-related sinus bradycardia occurred in (5%) of the nebivolol-using patients included in Group-1, where as in group-2 it was 1%.**Conclusion:** In patients with tachycardia caused angina, Ivabradine can be treated as the first alternative, as this heart rate reducer and chest pain agent. Nebivolol should be treated with the hypertensive tachycardia patient. Better findings are required for further analysis.**Keyword:** Coronary heart disease (CHD), Ivabradine, Nebivolol.**INTRODUCTION**

The recurrent condition is the atherosclerosis of the coronary artery. Acute heart disease will cause death in patients. In several European countries, death from coronary heart disease has declined markedly lately.

In developed nations, nearly 80% of deaths from all coronary artery diseases (CAD) occur. SAP is a commonly observed in CAD. New diagnostic and prognostic studies of SAP patients are being established.^[1-3]

Mortality has been shown to rise with the high heart rate in chronic heart failure (CHF) patients. Regarding CHF mortality, it was found that a 1-beat per minute rise in the cardiovascular rate raises the mortality risk by 3 percent, whereas a 5-beat cardiac increase increases the death risk by 16 percent.^[4]

Ivabradine inhibits the pacemaker If current by slowing the diastolic depolarization slope in sinoatrial node cells in a dose dependent fashion. When the available data

regarding ivabradine is examined, it can be seen that ivabradine has the potential to slow-down the development of atherosclerosis, correct ischemia, and reduce the frequency of angina attacks, the prevalence of fatal and non-fatal myocardial infarction, and the rate patient hospitalization Among the different betablockers, nebivolol is a cardio selective agent that has long-term efficacy.^[5]

In this study our main goal is to evaluate clinical outcome of Ivabradine and Nebivolol in the treatment of Stable Angina Pectoris Patients with mild left ventricular dysfunction.

OBJECTIVE**General objective**

- To assess clinical outcome of Ivabradine and Nebivolol in the treatment of Stable Angina Pectoris Patients with mild left ventricular dysfunction

METHODOLOGY

Study type

- It was a cross sectional study.

Place and period of the study

- This study was carried out Noakhali 250-Bed General Hospital from April 2020 to December 2020.

Method

- A total of 200 stable angina pectoris patients under follow-up in the cardiology department of Noakhali 250-Bed General Hospital with LVEFs 45% to 50% were included into the study. The patients were evaluated in 2 different groups.^[1,2] In group-1 Nebivolol 5mg/day was administered to the 100 patients included in Group A. 100 patients were started on Ivabradine 10mg/day and these patients were included into group-2. All patients admitted in Cardiology department, fulfilling the inclusion criteria and exclusion criteria was considered for study. Informed written consent was taken from all patients before enrollment. Initial evaluation of the patients by history and clinical examination was performed and recorded in patients' data collection sheet. Demographic profile, and pulse, blood pressure, body weight was recorded.

Statistical analysis

- The numerical data obtained from the study was analyzed and significance of differences was estimated by using statistical methods. Computer based SPSS (Statistical Package for Social Science) was used. Data is expressed in percentage, frequencies, means and standard deviation as applicable by simple linear analysis, Pearson χ^2 square test, Students't test, Pearson's correlation coefficient test, multivariate logistic regression

analysis and Fisher's exact test as applicable. P value of less than 0.05 was considered as significant.

RESULTS

In figure-1 shows age distribution of the patients where in group-1 most of the patients belong to 40-50 years' age group, 43% where as in group-2 majority belong to >50 years' age group, 46%. The following figure is given below in detail:

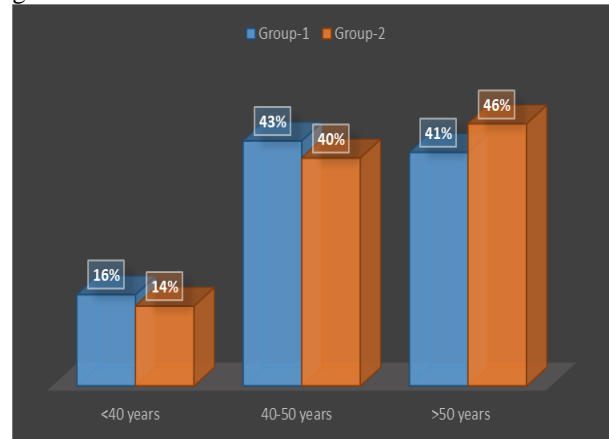


Figure 1: Age distribution of the patients.

In table-1 shows gender distribution of the patients where among the study male patients were highest than female population and the male and female patients were identical in both the groups which was statistically insignificant ($p=0.73$) by χ^2 (Chi square) test. The following table is given below in detail:

Table 1: Gender distribution of the patients.

Gender	Group-1, %	Group-2, %	P value
Male	95	90	0.73 ^{ns}
Female	5	10	

In table-2 shows distribution of the patients according to systolic Diastolic BP and heart rate where heart rate decreased (79±7) to (66±5.1) in Group: 1 and (78± 7) to (71 ± 5) in Group: 2. The following table is given below in detail:

Table 2: Distribution of the patients according to systolic Diastolic BP and heart rate.

Variable	Before treatment Group -1 (n = 50)	After treatment, Group -1 (n = 50)	Before treatment, Group-2 (n = 50)	After treatment, Group-2 (n = 50)
Systolic BP (mm Hg)	143 ± 1.3	123 ± 2.0	146 ± 1.9	130 ± 2.4
Diastolic BP (9mm Hg)	91 ± 2.4	81 ± 2.1	89 ± 2.2	84 ± 3.2
Heart rate	79±7.0	66±5.1	78± 7.0	71 ± 5.0

In table-3 shows improvement of EF in Group-1 and Group-2 where After 6 months' treatment LVEF for the group-1 improved by (45 ± 6.5) to (52 ± 3.1), and for the group-2 (48± 5.5) to (53 ± 2.1). There is no significant change in EF improvement in both groups. The following table is given below in detail:

Table 3: Improvement of EF in Group-1 and Group-2

Status of EF	Before treatment, mean	After six months, mean
Group-1	45 ± 6.5	52 ± 3.1
Group-2	48± 5.5	53 ± 2.1

In figure-2 shows dose-related side effects of the patients where dose-related sinus bradycardia occurred in (5%) of the nebivolol-using patients included in Group-1, where as in group-2 it was 1%. The following figure is given below in detail:

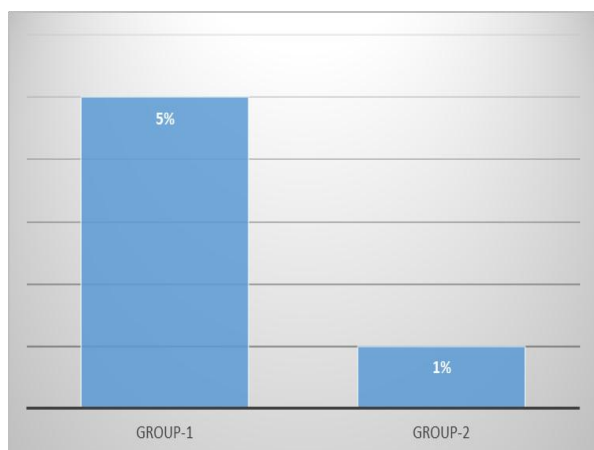


Figure 2: Dose-related side effects of the patients.

DISCUSSION

In our study, After 6 months' treatment LVEF for the group-1 improved by (45 ± 6.5) to (52 ± 3.1), and for the group-2 (48 ± 5.5) to (53 ± 2.1). There is no significant change in EF improvement in both groups. In one study said that, Ivabradine was reported as having no adverse effects on the LVEF.^[5]

The results of the one study have demonstrated that ivabradine is a good choice for antianginal and antiischemic treatment, that it reduces the incidence of myocardial infarction and the need for coronary revascularization, and that it has a good tolerability profile when used in combination with other drugs. This study has also shown that ivabradine use represents advancement in the treatment of stable angina pectoris patients with heart rates of ≥ 70 beats per minute, and that the isolated decrease in heart rate caused by ivabradine decreased the occurrence of coronary events even in patients already receiving optimal cardiovascular protective therapies.^[6] In their efficacy study on ivabradine and nebivolol combination therapy performed with 92 patients, they observed no difference between these two drugs with regards to antianginal, antiischemic and antitachycardia efficacy.^[7] The results of this study are in parallel with the above-mentioned studies.

In our study, the effects of the ivabradine and nebivolol mono therapies on the respiratory system were evaluated. According to our study's results, ivabradine has not demonstrated any effect that might lead to pulmonary dysfunction. It has been shown that ivabradine had no adverse effect on the pulmonary functions of patients with COPD and pulmonary hypertension in studies.^[6-7]

We observed that nebivolol had minimal effect on pulmonary dysfunction. The effects of the ivabradine and nebivolol mono therapies on diastolic dysfunction were evaluated in our patients. During the pre-treatment and the six month treatment periods, ivabradine's efficacy on the diastolic parameters was found to be equal to that of nebivolol. One study have conducted on 111 patients with EFs below 50% described ivabradine's effect in improving diastolic parameters on its own.^[8]

CONCLUSION

In patients with tachycardia caused angina, Ivabradine can be treated as the first alternative, as this heart rate reducer and chest pain agent. Nebivolol should be treated with the hypertensive tachycardia patient. Better findings are required for further analysis.

REFERENCES

1. Swedberg K, Komajda M, et al. Ivabradine and outcomes in chronic heart failure (SHIFT): A randomised placebocontrolled study. *Lancet*, 2010; 376: 875-85.
2. Kim Fox, Ian Ford, P Gabriel Steg, et al. Ivabradine for patients with stable coronary artery disease and left-ventricular systolic dysfunction (BEAUTIFUL): A randomised, doubleblind, placebocontrolled trial. *Lancet*, 2008; 372: 807-16.
3. Borer JS, Böhm M, Ford I, et al. Effect of ivabradine on recurrent hospitalization for worsening heart failure in patients with chronic systolic heart failure: The SHIFT Study. *Eur Heart J.*, 2012; 33:2813-20.
4. Tardif JC, Ponikowski P, Kahan T, ASSOCIATE Study Investigators. Efficacy of the I(f) current inhibitor ivabradine in patients with chronic stable angina receiving beta-blocker therapy: A 4-month, randomized, placebo-controlled trial. *Eur Heart J.*, 2009; 30: 540-48.
5. Tatarchenko IP, Pozdniakova NV, Biriuchenko MV, et al. Clinical efficacy of ivabradin and nebivolol addition in combined treatment of ischemic heart disease patients with left ventricular dysfunction. *J. Ter Arkh.*, 2008; 80: 40-44.
6. Akhmetzianova ÉKh, Ga-nitdinova VV, Bakirov AB, Bogoroditskaia OA, Timershina IR. Effect of ivabradine on pulmonary hypertension in chronic obstructive pulmonary disease. *Kardiologiya*, 2012; 52: 41-46.
7. Swedberg K, Komajda M, Böhm M, Borer JS, Ford I, Tavazzi L. Rationale and design of a randomized, double-blind, placebo-controlled outcome trial of ivabradine in chronic heart failure: the Systolic Heart Failure Treatment with the I(f) Inhibitor Ivabradine Trial (SHIFT), *Eur J Heart Fail*, 2010.
8. De Luca G. Ivabradine and diastolic heart failure. *Am Coll Cardiol*, 2012; 59: E1009. Fox K, Garcia MA, Ardissino D, et al. Guidelines on the management of stable angina pectoris: Executive summary: The task force on the management of stable angina pectoris of the European Society of Cardiology. *Eur Heart J.*, 2006; 27: 1341-81.