The efficacy of Ivabradine and Nebivolol in the Treatment of Stable Angina Pectoris Patients with Mild Left Ventricular Dysfunction

Dr. Md. Rafiqul Islam*

Abstract

Objective: In this study my main goal is to evaluate the efficacy 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 in tertiary medical college and hospital from December 2018 to December 2019. A total of 100 consecutive patients were included. The patients were evaluated in 2 different groups (1, 2). In group-1 Nebivolol 5mg/day was administered to the 50 patients included in GroupA. 50 patients were started on Ivabradine 10mg/day and these patients were included into group-2. Results: During the study, heart rate decreased (78±6) to (65±5) in Group: 1 and (77±7) to (70±5) in Group: 2. After 6 months’ treatment LVEF for the group-1 improved by (48±6.5) to (51±3.2), and for the group-2 (47±5.4) to (51±2.3). There is no significant change in EF improvement in both groups. Dose-related sinus bradycardia occurred in (5%) of the nebivolol-using patients included in Group-1, whereas in group-2 it was 1%. Conclusion: From my study I can conclude that, Ivabradine can be considered as first choice in patient with tachycardia induced angina as this agent for reducing heart rate as well as chest pain. The hypertensive patient with tachycardia may be treated by Nebivolol. Further study is needed better result. Keywords: Coronary heart disease (CHD), Ivabradine, Nebivolol.

INTRODUCTION

Atherosclerotic coronary artery disease is a chronic disease. Acute coronary syndrome can trigger patient mortality. Recently coronary artery disease mortality has decreased significantly in many European countries. About >80% of all coronary artery disease (CAD) deaths occur in developing countries. SAP is a clinical condition that is frequently encountered with CAD. New investigations are being developed for the diagnosis and prognosis of patients with SAP [1-3].

It has been shown that mortality in chronic heart failure (CHF) patient’s may increase in relation to an elevated heart rate. With regards to CHF mortality, it has been observed that an increase in heart rate of 1 beat per minute increases the mortality risk by 3%, while an increase in heart rate of 5 beats per minute increases the mortality risk by 16% [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 of patient hospitalization. Among the different betablockers, nebivolol is a cardioselective agent that has long-term efficacy [5].

In this study my main goal is to evaluate the efficacy of Ivabradine and Nebivolol in the Treatment of Stable Angina Pectoris Patients with Mild Left Ventricular Dysfunction.

OBJECTIVE

General objective

- To evaluate efficacy of Ivabradine and Nebivolol in the Treatment of Stable Angina Pectoris Patients with Mild Left Ventricular Dysfunction

Specific objective

- To identify cardiovascular risk factors of the patients.
- To detect dose-related side effects of the patients.
**METHODOLOGY**

**Study type**
- It was a cross sectional study.

**Place and period of the study**
- This study was carried out in tertiary medical college and hospital from December 2018 to December 2019.

**Method**
A total of 100 stable angina pectoris patients under follow-up in the cardiology department of tertiary medical college and 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 50 patients included in Group A. 50 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 x² 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 whereas in group-2 majority belong to >50 years age group. The following figure is given below in detail:

![Fig-1: Age distribution of the patients.](image)

In table-1 shows gender distribution of the patients where among the study population the male and female patients were identical in both the groups which was statistically insignificant (p=0.74) by χ² (Chi square) test. The following table is given below in detail:

| Gender | Group-1, n | Group-1, % | Group-2, n | Group-2, % | P value |
|--------|------------|------------|------------|------------|---------|
| Male   | 45         | 90.0       | 44         | 88.0       | 0.74**  |
| Female | 5          | 10.0       | 6          | 12.0       |         |

In table-2 shows distribution of the patients according to systolic Diastolic BP and heart rate where heart rate decreased (78±6) to (65±5) in Group: 1 and (77±7) to (70 ± 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) | 145 ± 1.2                         | 125 ± 2.1                         | 145 ± 1.8                         | 130 ± 2.4                         |
| Diastolic BP (9mm Hg) | 90 ± 2.5                           | 82 ± 2.1                          | 89 ± 2.2                          | 85 ± 3.2                          |
| Heart rate       | 78±6                              | 65±5                              | 77± 7                             | 70 ± 5                            |

In figure-2 shows improvement of EF in Group-1 and Group-2 where after 6 months’ treatment LVEF for the group-1 improved by (48 ± 6.5) to (51 ± 3.2), and for the group-2 (47 ± 5.4) to (51 ± 2.3). There is no significant change in EF improvement in both groups. The following figure is given below in detail:

![Fig-2: Improvement of EF in Group-1 and Group-2](image)

In figure-3 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:

![Fig-3: Dose-related side effects of the patients](image)

**DISCUSSION**

In my study, I have compared the effects of ivabradine and nebivolol in stable angina pectoris patients with mild LV systolic dysfunction (LVEF ≤50%). No notable differences were observed in comparisons of nebivolol and ivabradine monotherapies’ efficacy on the LVEF (nebivolol - LVEF 48 ± 6.5%; ivabradine - LVEF 47 ± 5.4). 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 cardiovascularprotective 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 is in parallel with the
above-mentioned studies.

In my study, the effects of the ivabradine and nebivolol mono therapies on the respiratory system were evaluated. According to my 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 a study [6].

I observed that nebivolol had minimal effect on pulmonary dysfunction. The effects of the ivabradine and nebivolol mono therapies on diastolic dysfunction were evaluated in my patients. During the pre-treatment and the six month treatment periods, ivabradine’s effect on the diastolic parameters was found to be equal to that of nebivolol. One study has conducted on 111 patients with EFs below 50% described ivabradine’s effect in improving diastolic parameters on its own [7].

CONCLUSION
From my study I can conclude that, Ivabradine can be considered as first choice in patient with tachycardia induced angina as this agent for reducing heart rate as well as chest pain. The hypertensive patient with tachycardia may be treated by Nebivolol. Further study is needed better result.

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