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A Study on Carvedilol versus Metoprolol in the Management of Atrial Fibrillation in Post Operative Coronary Artery Bypass Graft Surgery Patients

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ABSTRACT

The objective of the present study is to analyse the effectiveness of carvedilol and metoprolol in the management of atrial fibrillation in post operative coronary artery bypass graft surgery patients. Atrial fibrillation occurs frequently soon after coronary artery bypass grafting and often results in increased mortality and morbidity. The incidence of post operative atrial fibrillation actually varies from 11% to 40% despite of the surgical technique and current guidelines recommend beta blockers as a medication for the prevention of atrial fibrillation after coronary artery bypass graft surgery. A prospective observational study was conducted on 100 subjects considering the inclusion and exclusion criteria and they were classified into carvedilol and metoprolol group. Heart rate was chosen as the primary parameter and statistical analysis was performed using student't' test (p<0.05). There was a statistically significant decrease in the heart rate after therapy for both metoprolol and carvedilol but the difference in the effectiveness between carvedilol and metoprolol could not be significantly identified.

Keywords: Post Operative Atrial Fibrillation, Coronary Artery Bypass Graft Surgery, Metoprolol, Carvedilol, Heart Rate.

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INTRODUCTION

Atrial fibrillation is a supraventricular tachyarrhythmia characterized by uncoordinated atrial activation with subsequent deterioration of mechanical function. The incidence of atrial fibrillation after CABG surgery varies from 11% to 40%, with the arrhythmia usually occurring between the second and fourth postoperative days. [1] Postoperative atrial fibrillation has been

associated with a complicated postoperative course, increased incidence of stroke, increased length of hospital stay, increased hospital costs, in hospital and long-term mortality. [2-3] The pathophysiological mechanisms responsible for the high rate of atrial fibrillation after a cardiac surgery remains unclear even though mechanical damages to atrial structures, hypertension, increased volume, atrial ischemia due to the surgery, electrolyte imbalance, and pericardial injuries are some of the suggested involving factors. In spite of the fact that the impact of these factors on AF incidence is controversial, it has been approved that inflammation and oxidative injury to atrial tissue is higher during the surgery. [4] Given the clinical consequences attributable to POAF, its prevention is of great importance. To date, many pharmacologic approaches have been attempted to prevent POAF. [5-6] Although many approaches have been attempted to prevent postoperative atrial fibrillation, current guidelines suggest beta blockers as first-line medication to prevent postoperative atrial fibrillation after coronary artery bypass graft. [7] Metoprolol is a selective blocker of beta 1- receptor where as carvedilol is an alpha 1-adrenergic, beta1- adrenergic, and beta 2-adrenergic antagonist with ancillary antioxidant, anti-inflammatory, and antiapoptotic actions. [8-9] Both carvedilol and metoprolol have been used in the clinical setting for the prevention of atrial fibrillation but the recent data have suggested different pharmacological characteristics of carvedilol in comparison to other β-blockers. Therefore, we designed a randomized prospective observational trial that aimed to analyse and compare the effectiveness of carvedilol and metoprolol for the heart rate control in patients with atrial fibrillation following a coronary artery bypass graft surgery.

METHODS

Participants

This study included both male and female patients aged ≥ 18 years with persistent or permanent AF after the CABG surgery during the hospital stay and got treated with either metoprolol or carvedilol. The study excluded patients with psychiatric illness and other cardiothoracic vascular surgery patients.

Design

The study was a single centered, randomized, prospective observational study. The patients were divided into two treatment groups; group 1 included patients who received metoprolol for the control of AF and group 2 included those who received carvedilol. Both the groups were assessed continuously till discharge (7th post operative day).

The study was approved by the institutional review board of the participating institution, and it was conducted in accordance with the ethical principles defined in the Helsinki Declaration and Good Clinical Practice.

Outcome Measures

Using Holter ECG data and conventional method, the primary parameter: heart rate was noted (i) before the drug administration (ii) 24 hours after the drug administration and (iii) during the discharge. Observed data were entered into a standardized excel file.

Statistical Analysis

All continuous data were represented as means ± standard deviation. The paired 't' test was used to analyze the effectiveness of both drugs individually before and after drug administration using HR as the parameter. The unpaired 't' test was used to compare the effectiveness between the both drugs.

p value < than 0.05 was considered statistically significant. All statistics were performed using SPSS statistical version 24.

Table 1: Effectiveness of Metoprolol

	Mean Heart Rate	*P* value
Baseline heart rate	100.60 ± 11.79	0.000
Discharge heart rate	76.6 ± 8.98	

Table 2: 24 hours heart rate reduction by Metoprolol

	Mean Heart Rate	*P* value
Baseline heart rate	100.60 ± 11.79	0.063
Discharge heart rate	97.17±11.19	

Table 3: Effectiveness of Carvedilol

	Mean heart rate	*P* value
Baseline heart rate	97.6905 ± 11.4	0.000
Discharge heart rate	78.6905 ± 9.8	

Table 4: 24 hours heart rate reduction by Carvedilol

	Mean heart rate	*P* value
Baseline heart rate	97.6905 ± 11.4	0.795
Discharge heart rate	97.1429±12.56	

RESULTS

In this study, 118 patients underwent CABG surgery, out of which 100 patients received either Carvedilol (N=42) or Metoprolol (N=58).

Heart Rate Reduction by Metoprolol and Carvedilol

Two tailed tests and $p<0.05$ was used to confirm statistical significance. The heart rate before and after therapy with metoprolol and carvedilol was assessed individually using paired 't' test since it was the most accurate parameter to identify the effectiveness of beta blockers. There was a statistically significant decrease in the heart rate after therapy for both metoprolol and carvedilol ($p<0.05$).

After treatment with metoprolol, the mean heart rate was significantly reduced from the baseline heart rate (100.60 bpm) to 76.6 bpm at the time of discharge (Table 1, Figure 1). Also, the mean heart rate got reduced from the baseline heart rate after 24 hours of drug administration. Metoprolol has an immediate heart rate reduction effect (Table 2, Figure 2).

In carvedilol group, the mean heart rate was significantly reduced from the baseline heart rate 97.69 to 78.69 bpm at the time of discharge (Table 3, Figure 3).

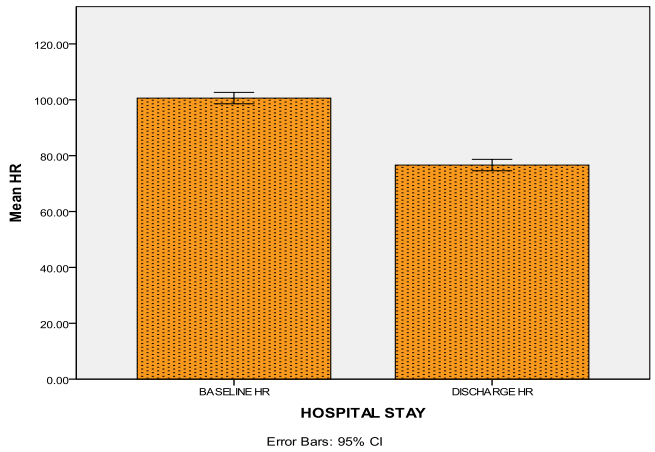

Fig. 1 : Effectiveness of Metoprolol

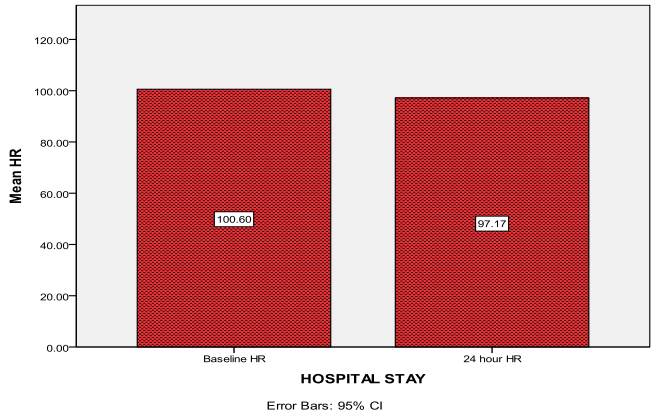

Fig. 2: 24 hours heart rate reduction by Metoprolol

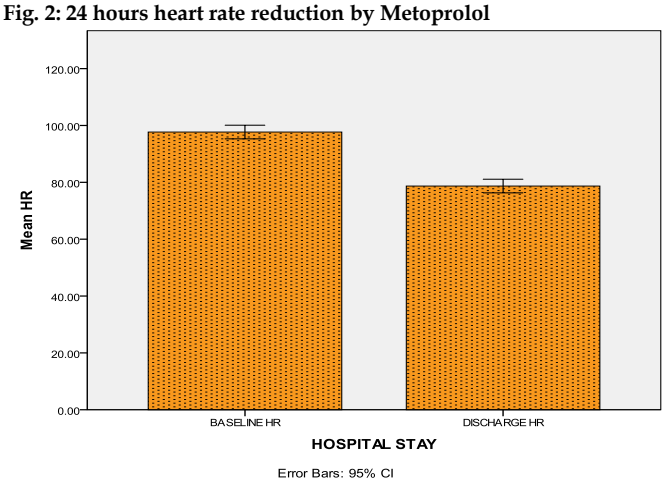

Figure 3: Effectiveness of Carvedilol

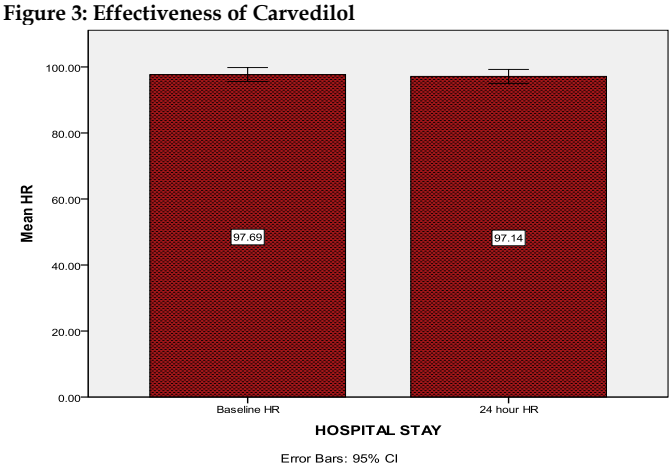

Figure 4 : 24 hours heart rate reduction by Carvedilol

And also the mean heart rate got reduced after 24 hours of administration of carvedilol (Table 4, Figure 4). Unpaired't' test was used to compare the effectiveness of metoprolol and carvedilol. The results showed a statistically insignificant difference in the effectiveness between carvedilol and metoprolol groups.

DISCUSSION

The incidence of CAD is generally high among the population as compared to the past due to several etiological reasons. And the occurrence of AF after CABG surgery varies from 11% to 40% with the arrhythmia usually occurring between the second and fourth postoperative days. Peak incidence was found on postoperative day two. [10] Updated American College of Cardiology/ American Heart Association (ACC/AHA) 2006 and 2014 guidelines strongly recommend preoperative or postoperative initiation of oral beta blocker therapy for the prevention of post CABG AF. Other recommended pharmacological prophylactic therapies include amiodarone and sotalol. [11-13]

Current study result shows mean heart rate was reduced for metoprolol and carvedilol from baseline with *p* value 0.000 (*p* value ≤ 0.05) which explains that both beta blockers are effective for post operative atrial fibrillation in CABG surgery patients. [13-14] But the difference in effectiveness between both drugs could not be explained by HR difference observed due to a statistically insignificant difference with *p* value ≥ 0.05. This was similar to *MacroMetra et al.* study in which the beneficial effects of carvedilol compared to metoprolol could not be explained by the differences in BP and HR observed after 4 months of study treatment or by patients not achieving target study drug levels. The heart rate achieved on maintenance beta blocker therapy and beta blocker dose have independent prognostic value. [15] This may be due to decreased sample size and limited time period. Metoprolol and carvedilol were significantly effective in reducing the heart rate but there was no statistically significant difference in the effectiveness when compared between two groups.

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