A Comparative Study on the Effect of Ranolazine and Ivabradine on High Sensitivity C-reactive protein In Cardiac Patients

Keywords: Ranolazine, Ivabradine, High sensitivity C-reactive protein

ABSTRACT
C-reactive protein (CRP) is a substance produced by the liver in response to inflammation. High CRP levels can indicate that there is inflammation in the arteries of the heart, which can mean a higher risk for heart attack. Ranolazine and Ivabradine are used in the treatment of cardiac problems such as angina, heart failure and in patients with acute coronary syndrome. These drugs have found to have action on C-reactive protein, which is a pentameric protein found in blood plasma whose levels rise in response to inflammation. Increased CRP levels indicate risk for atherosclerotic diseases. The aim of this study is to compare the effect of Ranolazine and Ivabradine on high sensitivity C-reactive protein in cardiac patients. Method: This is a prospective study going to be conducted in the department of cardiology, Pushpagiri Medical College Hospital, Thiruvalla. All patients who are willing to participate are explained about the brief study procedure. Approximately 60 patients will be taken for the study. The patients are selected based on the inclusion and exclusion criteria. Residual blood will be taken and is collected through the laboratory. The hsCRP levels can be analyzed by using semi auto-analyzer. The results obtained from the study can be compared with the normal range of hsCRP levels. Follow up will be conducted during the study period.
INTRODUCTION

C-reactive protein, it is a sensitive systemic marker of inflammation and tissue damage and is produced by hepatocytes predominantly under transcriptional control by the pro-inflammatory cytokine interleukin 6. C-reactive protein (CRP) is a non-specific biomarker for inflammation. Elevated serum levels of CRP using a high sensitivity assay (hsCRP) reflect subclinical inflammatory states such as vascular inflammation.

C-reactive protein (CRP) is a substance produced by the liver in response to inflammation. High CRP levels can indicate that there is inflammation in the arteries of the heart, which can mean a higher risk for heart attack. C-reactive protein is measured in milligrams of CRP per liter of blood (mg/L). CRP is traditionally measured down to concentrations of 3-5mg/L, whereas hs-CRP measures down to concentrations around 0.3mg/L. This improved sensitivity allows hs-CRP to be used to detect low levels of chronic inflammation. However, a desirable value is probably less than 1mg/ml.

Ranolazine is a novel antianginal drug. It acts by inhibiting a late sodium current in the myocardium which indirectly facilitates calcium entry through sodium-calcium exchanger. Reduction in calcium overload in the myocardium during ischemia decreases contractility and has a cardioprotective effect. Ranolazine has no effect on heart rate and blood pressure.

Ivabradine, a selective inhibitor of the funny current channel, reduces resting and exercise HR without affecting cardiac contractility or blood pressure. Funny current channels (If), are activated during the resting potential stage and accelerate diastolic depolarization of the sinus node and thus its pacemaker function. Ivabradine exerts antianginal and anti-ischemic effects in patients with coronary artery disease. Improved exercise tolerance, increased time to exercise-induced ischemia, and reduced frequency of ambient anginal attacks have been observed after funny current channel inhibition. Current research article is focused on comparison of the effect of Ranolazine and Ivabradine on high sensitivity c-reactive protein in cardiac patients.

REVIEW OF LITERATURE

Ahmed Fouad Abd EI Latif et al., (2015); conducted a study on The Effect of Ivabradine on Long Term Prevention of Major Adverse Cardiac Events in Acute Coronary Syndrome Using High Sensitivity C-reactive Protein. The aim of this study was to evaluate the influence of Ivabradine on long term prevention of major adverse cardiac events (MACE) using high.
sensitivity CRP. 60 patients were admitted to the CCU of critical care department at Cairo University presented with ACS over the period of 6 months. Cardiac enzymes were withdrawn on admission and every 6 hours thereafter for 24 hours then followed up daily for 5 days and when indicated. High sensitivity CRP (quantitative value) done on the day of admission and was repeated for follow up at day 4 and day 30 (after the withdrawal of study medication) with a normal range <0.5mg/dl. Patients were allocated randomly to the following groups; group A included 30 patients who received conventional therapy and Ivabradine. Group B included 30 patients who received conventional therapy only.

The result shows that significant variation in hsCRP value at day 30 in both groups (p-value <0.001). Patients of group A showed statistically significant lower level of hsCRP compared to group B. It has concluded that the administration of Ivabradine within 48 hours of CCU admission decrease the hsCRP levels in patients with ACS.

Adel et al., (2012); conducted a study on the “Clinical Study Evaluating The Effect Of Ivabradine On Inflammation In Patients With Non ST-segment Elevation Acute Coronary Syndromes”

This prospective, randomized, controlled, study recruited NSTE-ACS patients with HR ≥70beats per minutes. Each patient was randomly assigned to either control or ivabradine groups. The difference between the two groups was the addition of ivabradine (up to 7.5 mg bid) to the standard treatment of NSTE-ACS patients for 30 days in the ivabradine group. Levels of hsCRP were evaluated before and after the study period.

In this study 45 patients were enrolled, twenty three of which received ivabradine. The decrease (%) in HR after treatment was significantly larger in ivabradine group than in control group (23.8 (7.3 – 31) v/s 4.7 (0 - 22.5) %, p = 0.014). The decrease in HR was positively correlated to hsCRP reduction, r = 0.445, p = 0.003. No significant difference between ivabradine and control groups in hsCRP reduction (80 (38 - 90.6) v/s 61.3 (24 - 76.4) %, P = 0.057). Ivabradine was well-tolerated.

The study concluded that Ivabradine effectively and safely decreased HR in NSTE-ACS patients. Reduction in HR was associated with hsCRP reduction. Larger studies are required to better demonstrate the anti-inflammatory effects of ivabradine in ACS.

Rushworth et al. (2011); conducted a study on “Ivabradine: A New Rate-limiting Therapy For Coronary Artery Disease And Heart Failure.”
This study was first tested for efficacy in a cohort of 360 patients with stable angina. Antianginal efficacy and safety of ivabradine compared with amlodipine in patients with stable effort angina pectoris: a 3-month randomized, double-blind, multicentre, non-inferiority trial.

A subgroup analysis has shown that ivabradine improves mortality in patients with an initial heart rate greater than 70 bpm and because it can limit heart rate at rest and during exercise, it is particularly useful for treating ambulatory angina pectoris.

Ivabradine should currently be used as a second-line agent for managing angina, or as first-line treatment if the patient is intolerant to β-blockers or there are contraindications. Deshmukh et al., (2009); conducted a study on “Ranolazine Improves Endothelial Function In Patients With Stable Coronary Artery Disease”

The aim of this study was to investigate whether ranolazine, a novel antianginal medication with no effect on heart rate or blood pressure, improves endothelial function in patients with stable CAD. The objective was to find out the effect of ranolazine on endothelial-dependent vasodilation (EDV), serum markers of endothelial dysfunction and inflammation. This study comprises of 27 patients with stable CAD were randomly assigned to either 1000mg twice daily or to matching placebo for 6 weeks and then crossed over for an additional 6 weeks. The result showed that after 6 weeks, treatment with ranolazine significantly increased the EDV and a near significant decrease in C-reactive protein levels (p=0.05). Ranolazine improves endothelial function and C-reactive protein levels in a group of patients with stable CAD.

OBJECTIVES

-To compare the effect of Ranolazine and Ivabradine on high sensitivity C-reactive protein

-To evaluate the patient adherence and compliance with Ranolazine and Ivabradine

-To compare the clinical outcome of the drugs

-To estimate the quality of life in patients.

MATERIALS AND METHODS

A Prospective experimental study is planned to be conducted in the Department of Cardiology at Pushpagiri Medical College hospital, Thiruvalla, Kerala based on the topic “A
Comparative Study on the Effect of Ranolazine and Ivabradine on High Sensitivity C-Reactive Protein in Cardiac Patients.” 60 patients are planned to be selected for the study. The selection is based on the inclusion and exclusion criteria. Initially, the baseline hsCRP is to be taken within 24 hours of admission (before starting ranolazine or ivabradine therapy). The second value of hsCRP is to be taken after two weeks. For the determination of hsCRP, the residual blood will be collected from the laboratory and determined using semi-autoanalyzer in Pushpagiri College of Pharmacy, Kerala. Medication adherence will be analyzed by distribution of questionnaires according to ‘Morisky medication adherence scale.’ The quality of life will be estimated using the Minnesota Living with Heart Failure Questionnaire.

CONCLUSION

The high sensitivity CRP levels of patients taking either Ranolazine or Ivabradine can be evaluated. This study is done to identify which drug changes the levels of high sensitivity C-reactive protein and to suggest necessary modification in patients with cardiovascular disease.

REFERENCES

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