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A comparative study on the effect of Ranolazine and Ivabradine on high sensitivity C-reactive protein in cardiac patients

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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 the study was to compare the effect of Ranolazine and Ivabradine on high sensitivity C - reactive protein in cardiac patients. Method: This was a prospective study conducted in the Department of Cardiology, Pushpagiri Medical College Hospital, Thiruvalla. All patients willing to participate were explained about the brief study procedure. 60 patients were taken for the study. The patients were selected based on the inclusion and exclusion criteria. Residual blood was collected at the time of admission and after 2 weeks. The hsCRP levels were analyzed by using semi auto-analyzer. The results obtained from the study can be compared with the normal range of hsCRP levels. The effectiveness of Ivabradine and Ranolazine on hs-CRP levels reported that both the drugs decreased the hs-CRP levels. Ivabradine decreased hs-CRP levels more efficiently than Ranolazine.

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

INTRODUCTION

C-reactive protein is a sensitive systemic marker of inflammation and tissue damage and is

produced by hepatocytes predominantly under transcriptional control by the proinflammatory 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. [1] [2]

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. [5]

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. 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. [3][4][6]

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

This is a prospective experimental study conducted in 60 patients in the Department of Cardiology at Pushpagiri Medical College hospital, Thiruvalla. The patients were selected based on the inclusion and exclusion criteria. The drugs used in the study were Ranolazine and Ivabradine and the patients were randomly selected to receive Ranolazine 0.5g and Ivabradine 5mg. The study population was divided into two groups based on the administering drug. 30 patients were selected who were being administered with Ranolazine and 30 patients who were given Ivabradine. The patient's data were collected based on the demographic details. Initially the baseline hs-CRP was taken within 24 hours of admission (before starting ranolazine or ivabradine therapy). The second value of hs-CRP was taken at the time of discharge and it was then followed-up. For the determination of hs-CRP, the residual blood was collected from the laboratory and determined using semi-auto analyzer in Pushpagiri College of Pharmacy. After data collection, it was analysed using SPSS software. The results obtained on comparing the effects of Ranolazine and Ivabradine on hs-CRP and the results proved to reduce the elevated hs-CRP levels more were evaluated and documented. Medication adherence was analyzed by a distribution of questionnaires according to 'Morisky medication adherence scale'. Quality of life of patients was monitored using 'Quality of Life Enjoyment and Satisfaction Questionnaire'.

DETERMINATION OF HS-CRP

R1: Tris Buffer 20 mmol/L, pH 8.2, Preservative (sodium azide 0.95g/L)

Pipetted out 800 micro litre reagent by using a micropipette into a test tube

R2: Latex particles coated with goat IgG Anti human CRP, pH 7.3, Preservative (sodiumazide 0.95g/L)

Pipetted out 200 micro litre reagent and is added to the same test tube. Sample: Pipette out 5 micro litre of the patient serum and is added to the above Calibration Preparation: Add 1ml of distilled water into the CRP Calibrator. Calibrator: Liquid Calibrator, Human Serum.

Equation

$$n = \left(\frac{Z_{\alpha/2} \sigma}{E} \right)^2$$

Where,

Z = Standard value of confidence interval

σ = Standard deviation

E = Margin of error

RESULTS

In the 6 months study, a total of 60 patients were enrolled as per inclusion and exclusion criteria. All the patients were from the Department of Cardiology, Pushpagiri Medical College, Thiruvalla.

Table 1: Distribution of patients based on the effect of Ranolazine and Ivabradine on hs-crp levels (on admission and review)

	Hs-CRP LEVELS IVABRADINE (Mean Value)	RANOLAZINE (Mean Value)
ON ADMISSION	5.97	6.25
ON REVIEW	1.87	3.27

It was found out that the values on admission decreased in both the groups. The mean difference on admission and review for Ivabradine was 4.1

and for Ranolazine was 2.98. This indicated that Ivabradine had more efficiency in reducing hs-CRP levels than Ranolazine.

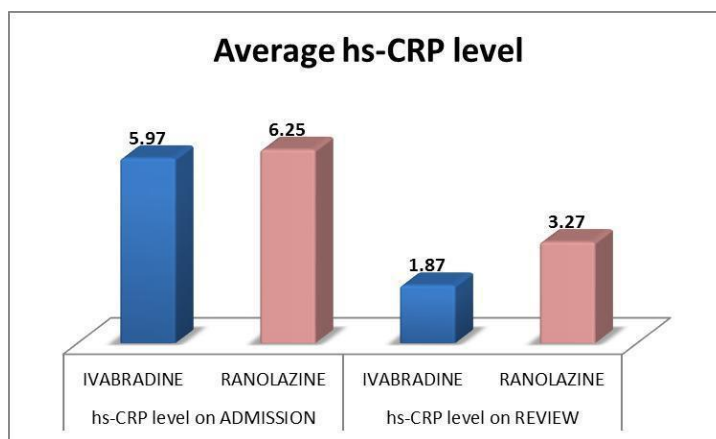
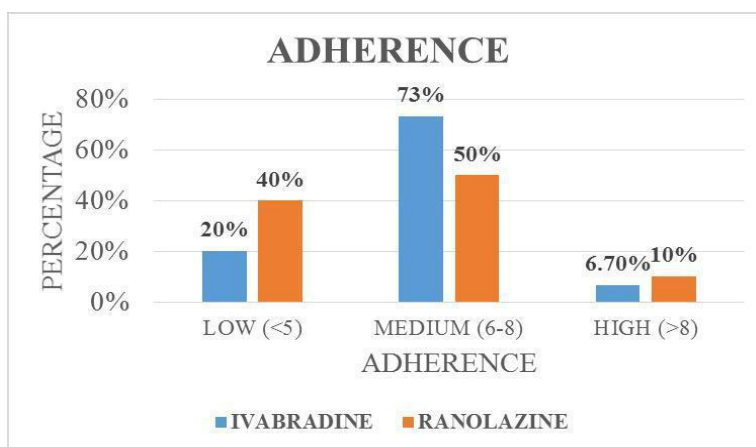


Figure 1: Distribution of patients based on the effect of Ranolazine and Ivabradine on hs-crp levels (on admission and review)

Table 2: Distribution of patients based on adherence

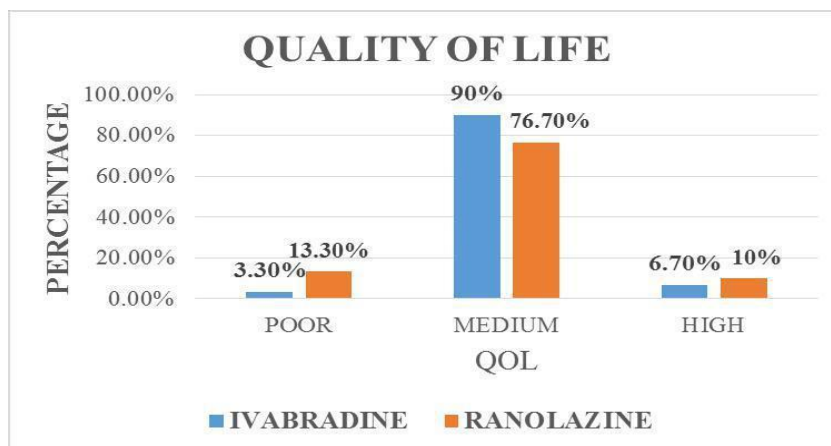
	IVABRADINE		RANOLAZINE		Pvalue
	FREQUENCY	PERCENTAGE	FREQUENCY	PERCENTAGE	
LOW (<5)	6	20.0%	12	40.0%	.172
MEDIUM (6-8)	22	73.3%	15	50.0%	
HIGH (>8)	2	6.7%	3	10.0%	

Among the study population, 30.0% showed low adherence, 61.7% showed medium adherence and 8.3% showed high adherence.

**Figure 2: Distribution of patients based on adherence****Table 3: Distribution of patients based on quality of life**

QUALITY OF LIFE	IVABRADINE		RANOLAZINE		P value
	FREQUENCY	PERCENTAGE	FREQUENCY	PERCENTAGE	
POOR	1	3.3%	4	13.3%	.313
MEDIUM	27	90.0%	23	76.7%	
HIGH	2	6.7%	3	10.0%	

Among the study population, 8.3% showed low quality of life, 83.3% showed medium quality of life and 8.3% showed high quality of life.

**Figure 3: Distribution of patients based on quality of life**

DISCUSSION

The study was conducted to find out the effect of Ranolazine and Ivabradine on hs-CRP levels. The residual blood sample of the patients were collected from the Biochemistry lab in order to find out the hs-CRP levels. The hs-CRP levels were found using semi auto analyzer in Pushpagiri College of Pharmacy, Thiruvalla. Patient's demographic details were analyzed. Medication adherence of the patients were also found out using Morisky Medication Adherence Scale. Quality of Life was measured using Quality of Life Enjoyment and Satisfaction Questionnaire. The data was collected from Cardiology department of Pushpagiri Medical College Hospital, Thiruvalla. Collected data was organized, tabulated and analyzed using SPSS software and described with the help of tables and graphs.

The patients involved in the study belonged to the 45 to above 75 age group. The mean age of the study population taking Ivabradine was 67 and Ranolazine was 69.

In the study population, 33.3% were females and 66.7% were males. 73.3% of males were taking Ivabradine and 60% were taking Ranolazine on the other hand 26.7% of Females were taking Ivabradine and 40% were taking Ranolazine.

The effects of Ranolazine and Ivabradine on hs-CRP levels on admission and on review were studied. In the case of Ranolazine, the mean hs-CRP level on admission and on review was found to be 6.25 and 3.27 respectively. In case of Ivabradine the mean hs-CRP level on admission and on review was found to be 5.97 and 1.87 respectively. The mean difference on admission and review for Ivabradine was 4.1 and for Ranolazine was 2.98.

In the group of patients taking Ivabradine majority of the patients were in the age group of 61-75 years (46.7%), while least was found in the group above 75 years (23.3%). The mean difference of hs-CRP levels in each age groups were calculated and it was found that the decrease in the hs-CRP in the Ivabradine group was more effective for the age group above 75 years (mean difference is 4.44).

In the group of patients taking Ranolazine majority of the patients were in the age group of 61-75 years (53.3%), while least was found in the group of 45-60 years (20.0%). The mean difference

of hs-CRP levels in each age groups were calculated and it was found that the decrease in the hs-CRP in the Ranolazine group was more effective for the age group above 75 years (mean difference is 3.18).

In patients taking Ivabradine, the mean difference of hs-CRP levels in case of female was 4.18 and that in males was 4.15.

But, in patients taking Ranolazine, the mean difference of hs-CRP levels in case of female was 2.6 and that in male was 2.48. Ivabradine was found more efficient in reducing hs-CRP levels in both females and males

SUMMARY

A prospective experimental study was conducted in the Department of Cardiology, Pushpagiri Medical College Hospital, Thiruvalla and Pushpagiri college of Pharmacy, Thiruvalla in order to compare the effect of Ranolazine and Ivabradine on high sensitivity C-reactive protein in cardiac patients. The total sample size of the study was 60 patients where the patients were divided into two groups of 30 patients each based on the administering drug, Ranolazine (0.5g) and Ivabradine (5mg). Patient's demographic details were collected and residual blood samples were analysed for hs-CRP values using semi-autoanalyser. Patient medication adherence was measured using Morisky Medication Adherence Scale and Quality of life evaluation was done using Quality of Life Enjoyment and Satisfaction Questionnaire. The study population belongs to the age group from 45 to above 75 and mean age was 67 for Ivabradine and 69 for Ranolazine. Also, about 66.7% of the population were males and 33.3% were females.

The first objective of our study was to compare the effects of Ranolazine and Ivabradine on hs-CRP levels in cardiac patients, for which the hs-CRP levels on admission and on review were studied and it was found that both the drugs decreased the hs-CRP levels.

The second objective of the study was to find out which drug was more effective in reducing hs-CRP values. The mean difference on admission and review for Ivabradine was 4.1 and for Ranolazine was 2.98. This indicated that ivabradine had more efficiency reducing hs-CRP levels than ranolazine

Our third objective was to evaluate medication adherence of the study population and patients were categorized into low (30%), medium (61.7%) and high (8.3%).

The fourth objective of our study was to evaluate Quality of life of the study population and patients were categorized into low (8.3%), medium (83.3%) and high (8.3%).

CONCLUSION

Inflammation plays a major role in atherothrombosis, and measurement of inflammatory

markers such as high-sensitivity C-reactive protein (hs-CRP), may provide a novel method for detecting individuals at high risk of cardiovascular disease.

The study carried out in Pushpagiri Medical College Hospital among the 60 subjects in order to compare the effectiveness of Ivabradine and Ranolazine on hs-CRP levels reported that both the drugs decreased the hs-CRP levels. Ivabradine decreased hs-CRP levels more efficiently than Ranolazine.

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