

Effect of Rivaroxaban in Stroke Prevention in Patient with Atrial Fibrillation Due to Valvular Heart Disease

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ABSTRACT

Objective: To observe the effect of rivaroxaban in patients with atrial fibrillation due to valvular heart diseases for proper anticoagulation to avoid stroke.

Methodology: An observational follow up study was carried out in Cardiology Department of Aziz Fatimah Hospital, Faisalabad from February to August 2021. The study included 36 patients of valvular heart disease with atrial fibrillation on warfarin, whose INR was not tested during the last 4 months due to lack of facility nearby. All patients with non-valvular atrial fibrillation were excluded. All patients were given rivaroxaban to replace warfarin. These patients were followed up for 6 months in the OPD of the same hospital to observe the end points including stroke and bleeding episodes and ischemic changes on ECG.

Results: Total of 36 patients of mean age and SD of 56 ± 7.00 years were followed up. Out of which 20 were male and 16 were female subjects. Not a single incident of stroke or bleeding episode or bruises was observed during the 6 months follow up. On echocardiographic examination, none of the patients showed clot in the left atrium. Left atrium size and LV ejection fraction remained the same, during next visit. LA size 44 ± 5 and 44 ± 6 on 1st and second visit respectively (p value = 0.059) No other ischemic changes found in the ECG of any patient. International normalization ratio (INR) mean and SD was 2.1 ± 0.9 , 2.2 ± 0.8 , on 1st and 2nd visit of follow up respectively and no significant difference were noted between INR values.

Conclusion: Rivaroxaban can be given safely to the patients with valvular heart disease with atrial fibrillation, particularly in patients who cannot get the INR checked on regular basis.

KEYWORDS: Atrial fibrillation, Rivaroxaban, Valvular heart disease.

INTRODUCTION

Atrial fibrillation is one of the most important cause of thrombo-embolic stroke in patients with valvular heart disease.^{1,2} Risk of thrombo-embolism increases

in patients who are not taking antithrombotic medicines properly.^{3,4} Effectiveness of treatment to prevent ischemic stroke, warfarin, can be checked by INR.⁵ Despite the use of warfarin, there are higher number of thrombotic strokes in patients with atrial fibrillation, probably due to the failure of checking the INR values on regular basis.⁶⁻⁸ In Pakistan, most of the patients living in the villages are either unaware or lack the nearby facility of getting this test done.^{9,10} Therefore, such patients usually get the complications due to the over dosage or under dosage of anticoagulation.¹¹ In this study we aimed to see the effect of rivaroxaban in preventing any thrombo embolic stroke, development of thrombus in the left atrium and assess its safety with regards to bleeding tendency with its use. Rivaroxaban is a fast acting, direct factor Xa inhibitor that disable the conversion of prothrombin to thrombin. Rivaroxaban is already licensed for use in stroke prevention in non-valvular atrial fibrillation, DVT, and pulmonary embolism.¹² The reason to conduct this study was to evaluate safety and efficacy of rivaroxaban in our population as conventionally used drug, warfarin requires strict monitoring by

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International Normalized Ratio (INR) which is not possible mostly in our population due to various reasons. The lack of local published data on the role of Rivaroxaban in the prevention of stroke in patients with atrial fibrillation due to valvular heart disease prompted us to carry out the present study

METHODOLOGY

An observational follow up study was carried out in Cardiology Department of Aziz Fatimah Hospital, Faisalabad from February to August 2021, after taking the ethical approval from institutional ethical committee with Ref.No: IEC/1143-21. We recruited 36 consecutive patients of valvular heart disease, particularly mitral stenosis with dilated left atrium reporting to outpatient department and indoor facility of Cardiology Department. These patients were with age 45 and above, having long standing persistent atrial fibrillation with a heart rate between 80 to 120 per minutes. All the patients had been taking warfarin for at least 4 to 6 months without having any access to the INR test facility nearby were included in this study. In this observational follow up study which included patients whose INR was not tested during the last 4 months. All patients aged less than 45 years of age and non-valvular atrial fibrillation were excluded from the study. Enrolled patients were put on oral rivaroxaban 15 mg once daily to replace warfarin.

Patients were instructed to contact immediately if they experienced any clinical evidence of stroke (symptoms were explained to the patients in details). These patients were then prospectively followed up for the next 6 months. During this follow up period, patients were assessed in the cardiology OPD with history, physical examination, ECG, chest X ray and Echocardiography after every 3 months. International Normalized Ratio (INR) was estimated and calculated as a ratio of the patient's PT to a control PT standardized for the potency of the thromboplastin reagent developed by the World Health Organization (WHO) using the following formula: $INR = \text{Patient PT} / \text{Control PT}$. Reference range for INR value from a score of 2.0 to 3.0 was considered normal.¹³

Electrocardiographic measurements:

Standard 12 lead electrocardiograms were recorded using a Hewlett Packard XLi Page Writer (Model M1700A) on a paper speed of 25 mm/s using calibration of 0.1 mV/mm. Parameters measured manually using electronic calipers (model no. CD-6" CP; Mitutoyo, UK Ltd).

Echocardiograms:

Echocardiography was performed by an experienced

cardiologist using Toshiba Nemio XG. Two-dimensional, and 2-D guided M-mode recordings of left ventricle (LV) were obtained from the conventional parasternal view with the patient in left semilateral position. Short axis and apical views were also obtained to examine the clot or thrombus. LV ejection fraction was estimated using the equation, $EF = (EDD^3 - ESD^3) / EDD^3 \%$.

Statistical Analysis: Stat view 5.0 (Abacus Concepts Inc. USA) for windows, a computer statistical package, was used to analyze the data. The data are presented as mean \pm standard deviation for counts. The Kolmogorov-Smirnov test was applied to confirm whether data followed the normal distribution. Differences in mean values and their significance were calculated using independent student t-tests after stratifying the assumptions. A probability value of less than 0.05 was taken as statistically significant.

RESULTS

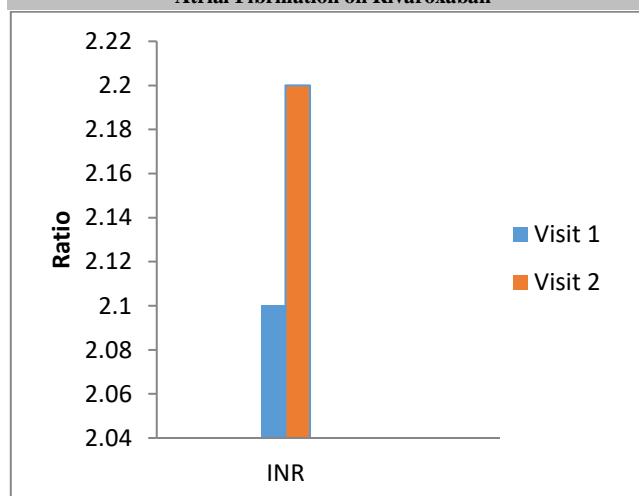
Total of 36 patients of mean age and SD of 56 ± 7.00 years were followed up. Out of which 20 were male and 16 were female subjects. One patient lost the follow up due to his immigration to another country.

Table 1: Basic characteristics of Patients (n= 36)

Characteristics	Mean \pm SD
Age (Years)	56 \pm 7.00
Systolic BP (mmHg)	130 \pm 14.00
Diastolic BP (mmHg)	80 \pm 6.00
Heart rate (beats/min)	90 \pm 12
LVEF in percentages	68 \pm 7

LVEF= left ventricular ejection fraction BP =blood pressure
SD=Standard Deviation

Figure 1: International Normalized Ratio (INR) of Patients With Atrial Fibrillation on Rivaroxaban



INR- International Normalization Ratio

DISCUSSION

Warfarin, a vitamin K antagonist is commonly used for prevention of thrombo-embolic phenomenon and stroke in patients with valvular and non-valvular atrial fibrillation.^{13,14} INR monitoring is most commonly recommended for the patients who are on warfarin. The dose of warfarin is adapted based on INR scores so that it remains in the therapeutic range to prevent thrombosis from subtherapeutic INR or hemorrhagic complications from supratherapeutic INR.¹³ It is always difficult to titrate the dose of Warfarin according to the required levels of INR. Despite monitoring and careful dose adjustment, INR values outside the target range are frequently observed.¹⁴ Now recent researchers are focusing on the Rivaroxaban, that has proven efficacy in stroke prevention in non-valvular atrial fibrillation in place of warfarin for stroke prevention in AF.¹⁵ Non vitamin K antagonists (NOACs) including rivaroxaban, as a group have been declared to have an edge over conventionally used vitamin K antagonist namely warfarin in several international guidelines.¹⁶ This study was conducted to evaluate the outcomes of Rivaroxaban prescribed to prevent stroke in patients with valvular heart disease, particularly mitral stenosis with dilated left atrium. We evaluate these for any type of episode of bleeding, bruises or stroke and INR value during the follow up. None of the followed-up patient showed any episode of bleeding, bruises or stroke in current study and INR remain unchanged and within normal range during follow up. On echocardiographic examination, none of the patients showed clot in the LA. Our results are justified by reporting of various researchers. Guimarães et al in their study on Brazilian population also found rivaroxaban to be safer and more effective than warfarin. Incidence of stroke was delayed by mean 347.5 days in patients on rivaroxaban as compared to mean 340.1 days in patients on warfarin.¹⁷ Furthermore, deaths from cardiovascular events in patients on rivaroxaban were also less (3.4%) as compared to those on warfarin (5.1%). Same conclusion was drawn by Barón-Esquivias et al in their review article comparing the safety and efficacy of rivaroxaban and warfarin in preventing stroke in patients with non-valvular atrial fibrillation.¹⁸ Gregory et al in a review article especially focused on Asian population with atrial fibrillation and found all NOACs including rivaroxaban to be safe in preventing stroke in patients with atrial fibrillation.¹⁹ All NOACs except rivaroxaban had lower hazard ratio in causing hemorrhagic stroke as compared to warfarin. This may be because of higher daily dose of rivaroxaban (20 mg) in this study whereas in our study the daily dose was

less (15 mg). Jaberi et al²⁰ studied the cost effectiveness of rivaroxaban in Iranian population in hospital-based study in city of Sheraz and concluded it to be more cost effective as compared to warfarin. Being newer molecule in Pakistan, there is very limited relevant data available. In a limited study by Haider. et al²¹ while studying rivaroxaban in patients with cerebral venous sinus thrombosis, found it to be safe and effective alternative to warfarin whereas in a similar study conducted at Rawalpindi Medical College, Rawalpindi, Pakistan by Maqsood. et al found no difference in terms of efficacy between rivaroxaban and warfarin to cause recanalization following cerebral venous sinus thrombosis.²²

Limitation: No doubt this is a medium sized study, the result cannot be generalized to such patients at large in clinical practice. Further research with bigger sample size of such patients with more prolonged follow-up is required in this regard.

CONCLUSION

Rivaroxaban can be given to patients with atrial fibrillation due to valvular heart disease particularly those who do not have access to INR test facility in immediate vicinity.

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Conflicts of Interest: None

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Authors' Contribution:

Dr. Waqar Shamim	Concept, literature search, data collection, analysis, first draft write- up.
Dr. M. Rizwan	Literature search, data collection, second draft write up.
Dr. Rizwan Rasul Khan	Study concept and design, analysis, final review, overall supervision.
Dr. Masood Javed	Literature search, study design & concept, data interpretation
Dr. Nasir Mahmood	Literature search, study design & concept, data interpretation
Dr. Kashif Nawaz	Literature search, data collection, drafting
	All authors are equally accountable for research work and integrity.

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