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ORIGINAL ARTICLE

Tolerability and Efficacy of Rivaroxaban vs Warfarin for Non Valvular Atrial Fibrillation

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Abstract

Introduction: Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia and is seen in 1–2% of the general population.

Objectives: The main objective of the study is to find the tolerability and efficacy of rivaroxaban Vs warfarin for non valvular atrial fibrillation.

Material and methods: This cross sectional comparative study was conducted in Pakistan Institute of Medical Sciences Islamabad during January 2021 to June 2021. After permission from hospital ethical committee, total 70 patients meeting the inclusion and exclusion criteria was enrolled in the study from OPDs of cardiology and allied Departments of hospital. Detailed history and physical examination was done to meet the inclusion and exclusion criteria. Informed consent was obtained.

Results: Out of 70 patients enrolled in total, 15 were excluded because of the above-mentioned exclusion criteria; 6 patients of NOAC group denied to participate and left cohort; and 4 patients lost the follow-up. Out of 45 participants, 21 were treated with rivaroxaban, while 24 were treated with warfarin.

Conclusion: It is concluded that oral anticoagulant drugs for prevention of stroke in non-valvular AF have been evolved and adding new options and advantages for patients and physicians such as fewer frequency of drug and food interactions, no need for monitoring, broad therapeutic index and tolerated better by patients.

INTRODUCTION

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia and is seen in 1–2% of the general population. The number of patients with AF in the United States was 2.2 million in 2010 and is expected to rise to 12 million by 2050. Ischaemic stroke and systemic thromboembolism are the most severe and fatal complications of AF. AF is responsible for 15% of the ischaemic stroke cases among all age groups and this rate increases up to 30% in people older than 80 years [1].

Warfarin is a vitamin K antagonist (VKA) that has been used in the prevention of AF for over 50 years. Randomised trials have shown that warfarin is superior to placebo, aspirin and the combination of aspirin clopidogrel in preventing stroke. Warfarin use is challenging due to its narrow therapeutic index and it has many food and drug interactions [2]. Thus, only 50 to 60% of the patients with AF are prescribed warfarin therapy and in 30 to 50% of these patients the international normalised ratio (INR) levels cannot be maintained within the therapeutic index. Although the efficacy of warfarin and other VKAs has been proven, the low and suboptimal use has led to the development of novel oral anticoagulants (NOACs) [3].

Warfarin sodium, a vitamin K antagonist, has been a mainstay of therapy to reduce thromboembolic stroke risk in patients with atrial fibrillation (AF), but it substantially increases the risk of intracranial and extracranial hemorrhage and it can be difficult to maintain patients in the therapeutic range [4]. Dabigatran etexilate mesylate, a direct thrombin inhibitor, and rivaroxaban, a factor Xa inhibitor, are non–vitamin K antagonist oral anticoagulants (NOACs), which are simpler to dose than warfarin and do not require therapeutic monitoring. In the Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) trial, dabigatran treatment was superior to warfarin treatment for reduction of stroke and intracranial hemorrhage (ICH) in patients with nonvalvular AF but was inferior for major gastrointestinal bleeding, in which risk was increased [5].

In the Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared with Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation (ROCKET-AF), rivaroxaban treatment was noninferior to warfarin treatment for prevention of stroke or systemic embolization. Intracranial and fatal bleeding events were reduced while major gastrointestinal bleeding was increased in the rivaroxaban arm [6].

Objectives: The main objective of the study is to find the tolerability and efficacy of rivaroxaban Vs warfarin for non valvular atrial fibrillation.

MATERIAL AND METHODS

This cross sectional comparative study was conducted in Pakistan Institute of Medical Sciences Islamabad during January 2021 to June 2021.

Sample Size: 70 patients (35 in each group) calculated with precision formula

$$n = \frac{\left\{ z_{1-\alpha}\sqrt{2\bar{P}(1-\bar{P})} + z_{1-\beta}\sqrt{P_1(1-P_1)+P_2(1-P_2)} \right\}^2}{(P_1-P_2)^2}$$

Where,
α = level of significance (1%)
β = power of study (99%)
P_1 = 0.25 (population in Group I)
P_2 = 0.75 (population in Group II)
n = 70 (35 in each group)

Sample Selection:

Inclusion criteria:

- Age between 18 to 60 years.
- Both male and female.
- Patients diagnosed with non valvular AF.
- Clinically stable patients.

Exclusion criteria:

Chronic kidney disease pateints

- Pregnant Females.
- Already taking any other drugs or suffering from any renal disease.
- Diabetic patients.
- Patients who are not willing to give consent

Data Collection Method: After permission from hospital ethical committee, total 70 patients meeting the inclusion and exclusion criteria was enrolled in the study from OPD of cardiology and allied Medical Departments of hospital. Detailed history and physical examination was done to meet the inclusion and exclusion criteria. Diagnosis was made with a clinical presentation consistent with non valvular AF. Informed consent was obtained.

The data was collected into two groups:

Group I: Treated with Rivaroxaban

Group II: Treated with Warfarin

Group I patients had given rivaroxaban 10-20 mg daily depending upon patients condition and subject to treating physician discretion and Group II patients had given 5-10mg of warfarin daily depending upon INR throughout the treatment period. Diagnosis was made with a clinical presentation consistent with AF. Both the groups were followed during hospitalization and after discharge of the patient for 30 days for the development of any complications. Post discharge follow up was done telephonically and in weekly OPD follow up personally to the patient or close relative of the patient as focal person.

Statistical Analysis: All the data was analysed by SPSS (Statistical Package for social sciences release 20.0; SPSS, Inc; Chicago, IL) system for Windows. Continuous variables expressed as mean ± SD (Standard deviation) while categorical variables expressed as frequencies and percentages.

RESULTS

Out of 70 patients enrolled in total, 15 were excluded because of the above-mentioned exclusion criteria; 6 patients of NOAC group denied to participate and left cohort; and 4 patients lost the follow-up. Out of 45 participants, 21 were treated with rivaroxaban, while 24 were treated with warfarin. Median age was 26 years in the group I and 25.3 years in the group II (p=0.705). Female cases counted for 18 (86%) and 19 (79%) in I and II groups, respectively. Risk factors, clinical presentation, affected vessels and brain lesions for both groups are depicted in Table I. Results from both groups were comparable and statistically no significant differences were observed (p•value more than 0.05).

Table 1: Demographic characteristics of selected patients

Baseline characteristics	All patients	Rivaroxaban	Warfarin	p-Value
AGE (mean, min-max)	25.3 (15–45)	26 (15–36)	27 (15–45)	
GENDER				
Male	08 (18%)	03 (14%)	05 (21%)	
Female	37 (82%)	18 (86%)	19 (79%)	
RISK FACTOR				
OCP	08 (18%)	03 (14%)	05 (21%)	.613
Anemia	13 (29%)	06 (29%)	07 (29%)	
Dehydration	06 (13%)	04 (19%)	02 (08%)	
Pregnancy/Puerpureum	22 (49%)	10 (48%)	12 (50%)	
Unknown Factor	07 (16%)	03 (14%)	04 (17%)	
Thrombophilia	04 (09%)	01 (05%)	03 (13%)	
Ischemic stroke	25 (56%)	12 (57%)	13 (54%)	.843
Hemorrhagic stroke	17 (38%)	08 (38%)	09 (38%)	.968
Myocardial infarction	13 (29%)	06 (29%)	07 (29%)	.965
Intracranial hemorrhage	17 (38%)	08 (38%)	09 (38%)	.968
Duration (months) mean (min-max)	03 (03–12)	03 (03–12)	03 (03–12)	.058

Table 2: Complications and clinical outcomes in both groups

VARIABLES	All Patients	Rivaroxaban	Warfarin	p-Value
At 3 months				
Overall	32 (71%)	15 (71%)	17 (71%)	.377
Partial	11 (24%)	03 (14%)	08 (33%)	
Complete	21 (47%)	12 (57%)	09 (38%)	
At 6 months				
Overall	38 (84%)	18 (86%)	20 (83%)	.598
Partial	10 (22%)	04 (19%)	06 (25%)	
Complete	28 (62%)	14 (67%)	14 (58%)	
At 12 months				
Overall	45 (100%)	21 (100%)	24 (100%)	.754
Partial	05 (11%)	02 (10%)	03 (13%)	
Complete	40 (89%)	19 (90%)	21 (87%)	
All bleeding events	08 (18%)	02 (10%)	06 (25%)	.161
Clinically non relevant minor bleeding	06 (13%)	02 (10%)	04 (17%)	
Clinically relevant non major bleeding	02 (4%)	00	02 (8%)	
Major bleeding	00	00	00	

DISCUSSION

Although there are several studies regarding the cost-effectiveness of NOACs (novel/new oral anticoagulants) in the prevention of recurrent stroke due to non valvular atrial fibrillatin(NVAF) in high-income countries [8], as far as we know, the current study is one of the few concerning this issue in lower middle-income countries (LMICs) . The study is aimed at evaluating new oral anticoagulant strategies for the prevention of ischemic stroke from a societal perspective [9].

The results obtained in the present study indicated that the use of rivaroxaban in the treatment of NVAF patients was associated with fewer disabilities than the treatment with warfarin [10]. Specifically, the patients undergoing the treatment with rivaroxaban were in a better condition in terms of moving around, self-care, daily activities, pain, and discomfort, as well as anxiety and depression compared to the patients treated with warfarin, which led to a decline in the mean score [11].

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia. Ischemic stroke and systemic thromboembolism are the most fatal complications of AF. Vitamin K antagonists (VKA) are used in the prevention of AF-related stroke and systemic thromboembolism. However, the use of VKAs is associated with limitations such as their narrow therapeutic index, the need for monitoring, and numerous food-drug interactions [12].

CONCLUSION

It is concluded that oral anticoagulant drugs for prevention of stroke in non-valvular AF have been evolved and adding new options and advantages for patients and physicians such as fewer frequency of drug and food interactions, no need for monitoring, broad therapeutic index and tolerated better by patients.

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