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ORIGINAL ARTICLE

Role of Different Oral Anticoagulants Used During Diabetes-Related Complications in Patients with Atrial Fibrillation

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ABSTRACT

Introduction: Globally, cardiovascular disease is the main contributor to mortality, accounting for about 17.5 million deaths, or 46.2% of deaths from non-communicable diseases.

Objectives: The main objective of the study is to find the diabetes-related complications and mortality in patients with atrial fibrillation receiving different oral anticoagulants.

Material and methods: This cross-sectional study was conducted in Pakistan Institute of Medical Sciences, hospital Islamabad from August 2021 to May 2022. The data were collected from 120 diabetic patients who were diagnosed with AF. After permission from the hospital ethical committee, a total of 120 patients meeting the inclusion and exclusion criteria was enrolled in the study. A detailed history of DM and physical examination were done to meet the inclusion and exclusion criteria.

Results: The data were collected from 120 patients. Out of 120 participants, 60 were treated with warfarin while 60 were considered as the control group. The median age was 26 years in group I and 25.3 years in group II (p=0.705). Female cases counted for 41 (86%) and 19 (14%) in the I and II groups, respectively.

Conclusion: It is concluded that patients with AF and diabetes have a high overall cardiovascular risk. Non–vitamin K antagonist oral anticoagulants were associated with lower hazards of diabetes complications and mortality than warfarin in patients with AF and DM.

INTRODUCTION

Globally, cardiovascular disease is the main contributor to mortality, accounting for about 17.5 million deaths, or 46.2% of deaths from non-communicable diseases. Atrial fibrillation (AF) is present in approximately 3% of the general adult population and its prevalence is expected to increase, particularly as a result of population aging [1]. With an estimated future increase in the number of people with AF from 14 to 17 million in Europe by 2030, together with an associated fivefold increased risk of stroke and twofold increased risk of mortality, AF will have a significant impact on the future. health care costs [2].

Diabetes mellitus is known as an acute disease which is really a leading public disease. It affects about two to five percent of the adult population in developed countries. The rate of type 2 diabetes is expected to increase in more than a decade, as well as the fact that revealed that 425 million individuals worldwide currently have diabetes, and even more than thirty-nine million people in the MENA region; this will increase to 67 million by 2045. In 2017, there were 7,474,000 cases of diabetes in Pakistan [3].

Both atrial fibrillation (AF) and diabetes mellitus (DM) are health conditions that epidemically affect Western populations today. These diseases have evolved into a serious health threat and a costly global health burden [4]. AF is the most clinically significant heart rhythm disorder; its prevalence will increase to 16 million by 2050. At the same time, individuals with DM have an approximately 40% higher risk of AF than their non-diabetic counterparts [5]. Well-documented cardiovascular (CVD) risk factors place individuals at risk of developing both AF and DM, although the exact etiology of this relationship has long eluded our understanding [6].

Over the years, numerous studies have investigated the effect of DM on the prognosis of AF and the effectiveness of its treatment. However, the relationship between FS and DM still remains a promising area of study as there is increasing evidence that their co-occurrence influences and confounds clinical outcomes. Despite a large number of studies on AF and DM, there are still insufficient data on blood glucose regulation as a prognostic modifier in DM patients with AF [7].

Rivaroxaban and apixaban are currently the most commonly initiated NOACs, but no direct randomized trial has directly compared the 2 drugs. Both drugs are factor Xa inhibitors, but have different pharmacokinetic profiles that could affect their safety and efficacy [6]. Although several observational studies have compared apixaban and rivaroxaban in patients with AF, these studies are prone to treatment selection bias due to unmeasured patient characteristics important for treatment choice. Apixaban is likely to be preferred over rivaroxaban in patients with low renal function and high risk of bleeding, and these characteristics are only partially recorded in registries. Instrumental variable (IV) methods, in which a factor (instrument) predicts treatment choice but does not directly affect outcomes, can address unmeasured confounding [7].

Warfarin is a vitamin K antagonist (VKA) that has been used in the prevention of AF for more than 50 years. Randomized trials have shown that warfarin is superior to placebo, aspirin, and aspirin-clopidogrel in preventing stroke. Taking warfarin is challenging due to its narrow therapeutic index and many food and drug interactions. The number of patients with atrial fibrillation (AF) in need of stroke prevention continues to rise [2]. The prevalence of AF increases with age and is associated with a higher risk of ischemic stroke. The use of warfarin reduces the risk of ischemic stroke in patients with AF, but they need frequent monitoring and dose adjustment. Ischemic stroke is considered a focal neurological deficit from non-traumatic and non-hemorrhagic causes. AF is the cause of ischemic stroke in 15% of all age groups and 30% of people over 80 years of age. The risk of ischemic stroke increases significantly with discontinuation of anticoagulants [3].

Objectives: The main objective of the study is to find the diabetes-related complications and mortality in patients with atrial fibrillation receiving different oral anticoagulants.

MATERIAL AND METHODS

This cross-sectional study was conducted in Pakistan Institute of Medical Sciences, hospital Islamabad from August 2021 to May 2022. The data were collected from 120 diabetic patients who were diagnosed with AF.

Inclusion criteria:

- Age between 18 to 60 years.
- Both male and female.
- Patients diagnosed with DM with AF.

Exclusion criteria:

- Already taking any anticoagulant drug

- Patients suffering from renal disease.
- Any bleeding disorder.
- Patients who are not willing to give consent

Data Collection Method: After the approval of the hospital ethics committee, a total of 120 patients meeting the inclusion and exclusion criteria were included in the study. A detailed DM history and physical examination were performed to meet the inclusion and exclusion criteria. Informed consent was obtained.

The data was collected into two groups:

Group I: Warfarin treatment

Group II: Control group (treated with Rivaroxaban)

Group I patients were treated with warfarin 15 mg daily twice daily for one month, then 20 mg daily for 5 months throughout the treatment period, and group II patients with rivaroxaban 15 mg daily twice daily for one month, then 20 mg daily for 5 months. The diagnosis was established with a clinical picture of DM consistent with FS. Both groups were monitored during hospitalization and after discharge for 30 days for the development of any complications. Efficacy was defined as ischemic stroke or systemic embolism. Safety was defined as intracranial bleeding or gastrointestinal bleeding. Post-discharge follow-up was done monthly on an OPD basis.

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

RESULTS

Data were collected from 120 patients. Of the 120 participants, 60 were treated with warfarin, while 60 were considered the control group. The median age was 26 years in group I and 25.3 years in group II (p=0.705). In women, 41 (86%) and 19 (14%) were in group I and II. Risk factors, clinical presentation, affected vessels and AF for both groups are shown in Table I. Results from both groups were comparable and no statistically significant differences were observed (p• value more than 0.05).

Table 1: Demographic characteristics of selected patients

Baseline characteristics	All patients	Warfarin	Rivaroxaban	p-Value
AGE (mean, min-max)	25.3 (15–45)	26 (15–36)	27 (15–45)	
GENDER				
Male	13 (18%)	14 (14%)	15 (21%)	
Female	47 (82%)	46 (86%)	45 (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

Mean weight was 75.63 ± 8.35 cm. Most of the patients 64 (58.12%) were with the BMI of ≤30 kg/m^2.

Table 2: Percentage of patients according to BMI (n=120).

BMI	Group A (n=60)		Group B (n=60)		Total (n=120)	
	No. of patients	%age	No. of patients	%age	No. of patients	%age
≤30 kg/m^2	34	58.18	34	58.18	68	68.12
>30 kg/m^2	26	41.82	26	41.82	52	41.82
Mean ± SD	29.15 ± 3.42		29.05 ± 3.34		29.12 ± 3.41	

The P-value of the gender male was 0.027 and female was 0.159. Female showed more positive results than male in both Group A and group B. The number of patients in both groups were 55.

Table 3: Stratification of drug efficacy with respect to gender.

Gender	Group A (n=60) Efficacy		Group B (n=60) Efficacy		P-value
	Yes	no	yes	No	
Male	22	04	15	11	0.027
Female	26	08	22	12	0.159

DISCUSSION

Lifestyle modification is a new and highlighted treatment domain in the guidelines. . In patients with diabetes, several lifestyle factors may contribute to AF, such as obesity, physical inactivity and, as our study shows, excessive alcohol consumption in younger age groups and the subsequent worse prognosis associated with it, and multifactorial interventions are indeed important in the prevention of diabetes complications. 7]. In the small randomized trial ARREST-AF, in which 17% of patients with AF had known diabetes, a multifactorial intervention reduced the risk of recurrent AF.10 In the recent LEGACY trial, in which approximately 30% of patients had diabetes and 10% had impaired glucose tolerance, sustained weight loss reduced burden of recurrent AF [8]. Interestingly, a concomitant improvement in echocardiographic abnormalities was found with a reduction in left atrial volume and left ventricular septal thickness [9]. A similar effect as the outcome of a multifactorial intervention in AF was reported in a recent single-center study from Australia [10]. These studies were too small to evaluate the effect in subgroups with diabetes and AF, but since the clustering of cardiovascular risk factors is even more pronounced in patients with diabetes, there are reasons to believe that such a multifactorial intervention could be even more beneficial for these patients. patients. We found the highest frequency of events in patients treated with insulin [11]. The most likely explanation is that insulin treatment is a substitute for a longer duration of diabetes, which is supported by a recent nationwide study from Denmark, which reported higher mortality and risk of thromboembolism with longer duration of diabetes in patients with AF [12]. Due to the observational nature of our study, it cannot be concluded that insulin per se is responsible for the adverse outcome, rather that insulin use signifies a high-risk individual. There are several possible explanations for the increased risk of AF and subsequent cardiovascular events in patients with diabetes. Risk factors associated with metabolic syndrome and diabetes, such as hypertension, coronary heart disease, obesity, and arterial stiffness, are all individually associated with an increased risk of AF as well as the development of cardiovascular complications [13]. At the myocardial level, several mechanistic explanations have been proposed as a consequence of diabetes, including structural, metabolic, electrical, and electromechanical changes in atrial remodeling [14]. In addition, diabetes can lead to the development of diabetic cardiomyopathy and heart failure with preserved or reduced ejection fraction, which increases the risk of AF and worsens the prognosis [15].

CONCLUSION

It is concluded that patients with AF and diabetes have a high overall cardiovascular risk. Oral anticoagulants without vitamin K antagonists were associated with a lower risk of diabetic complications and mortality than warfarin in patients with AF and DM. Treatment with rivaroxaban 20 mg once daily was associated with a statistically significant increase in major extracranial bleeding, including major gastrointestinal bleeding.

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