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Use of Novel oral anticoagulants (NOACs) in patients with risk of stroke in non valvular Atrial Fibrillation (AF)

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Abstract

Background: Warfarin was used for decades to prevent stroke in high risk AF patients, recent guidelines and published data is recommending use of NOACs like Rivaroxaban as an alternative to Warfarin, Its use is increasing world over because of its predictable action, less food and drug interaction and no need of monitoring for dose adjustments, considering these facts we planned to conduct a study to see the frequency of use of Rivaroxaban in our local population of AF patients with risk of stroke calculated by CHA2DS2-VASc score.

Method: This cross-sectional study was done at National Institute of Cardiovascular disease (NICVD) from May 2017 to September 2017 included 137 non-valvular AF patients with high risk of stroke calculated by applying CHA2DS2-VASc score more than or equal to 2. Clinical details and information about anticoagulant medications prescribed to them was also obtained. SPSS 19 was used for the analysis, descriptive statistics such as mean ±SD, frequency and percentages were calculated. Z-test, t-test, and chi-square test were used for the assessment and comparison of data. Two sided p-value of 0.05 was considered for statistical significance.

Results: Total 137 patient were included 50.4% (69) were male, 104 (75.91%) out of 137 were on Anticoagulant therapy, with 86 (62.77%) were on Warfarin and only 18 (13.14%) were taking Rivaroxaban.

Conclusion: Our study showed very small percentage of non valvular AF patients with risk of stroke were prescribed Rivaroxaban. It's important to update our treating Physicians about this novel agent which is shown to be equally effective and safe in comparison to warfarin, and easy to prescribe without monitoring to reduce stroke risk.

Keywords

Novel oral anticoagulants (NOACs), Rivaroxaban, Non valvular atrial fibrillation

Introduction

Vitamin K antagonist like warfarin is recommended for years[1-3] for prevention of stroke in high risk non-valvular Atrial Fibrillation (AF) patients. Its benefits are related to achieving an optimal level of anticoagulation, considering its narrow therapeutic index, food and drug interactions, with frequent monitoring of International Normalization Ratio (INR) for dose adjustments leads to difficulty in starting and continuing this drug in clinical practice even in conditions where its indicated[4,5,6].

NOACs like Rivaroxaban, have more predictable anticoagulant effects, lesser food and drug interactions in comparison to vitamin K antagonists[7, 8]. All recent guidelines are considering Rivaroxaban to be a substitute to Warfarin in non-valvular AF patients with risk of stroke as it is found

to be non-inferior in effectivity and safety as Warfarin in a number of recent clinical trials [9-12]. One local study done by Ikramullah et al. showed only 27.5% of AF patients with high risk of stroke according to CHA2DS2VASc scoring system were treated with oral anticoagulation and all of them were taking Warfarin, it included two valvular patients as well[13]. This shows an inhibition towards prescribing oral anticoagulants in these high risk patients probably due to limitation we have with Warfarin use, as at present (NOACs) like Rivaroxaban is available in our country so we planned to conduct a study to see the present frequency of its use in Non-valvular AF patients with high risk of stroke.

Methodology

This cross-sectional study was conducted at National Institute of Cardiovascular Disease (NICVD) Karachi, Pakistan from May 2017 to September 2017 after getting approval of ethical review committee. Admitted or out patients above 20 years of age, with ECG evidence of paroxysmal, persistent or permanent Atrial fibrillation (AF) without any structural heart defect like hypertrophic and restrictive cardiomyopathy, constrictive pericarditis, valvular or congenital heart disease, having no evidence of thyroid disease or malignancy and without indications of anticoagulation other than AF and at high risk of stroke (CHA2DS2 VASc Score of more than or equal to 2) were selected. Informed consent was taken and all patients were inquired about their baseline clinical characteristics and Antithrombotic treatment they are prescribed. The CHA2DS2-VASc score was calculated by assigning 1 point each for Congestive Heart Failure (left ventricular ejection fraction [LVEF] ≤40%), hypertension, diabetes, vascular disease, age 65 years, and female gender, and 2 points for past history of thromboembolism(TE)/Transient Ischemic Attack (TIA)/stroke and for age ≥75 years. Information about different types of Antithrombotic therapies or medication like warfarin, (NOACs) like Rivaroxaban, etc. was also obtained from all patients.

Statistical Analysis:

Statistical package for social sciences (SPSS 21) was used to analyze the data. Mean ± SD was calculated for quantitative variables and frequency and percentages for categorical variables. Z-test or t-test was applied to test the hypothesis of equality of proportions or mean. Two-sided p-value of <0.05 was taken as criteria for statistical significance.

Results

This study includes 137 consecutive selected patients with high risk of stroke (CHA2DS2 VASc Score of more than or equal to 2), presented in outpatients department and admitted to National Institute of Cardiovascular Diseases (NICVD), Karachi Pakistan. Out of 137 patients 50.4% (69) were male, mean age 62.08 ± 10.91 years. Hypertension, CHF ≤ 40%, vascular disease, diabetes, and stroke / TIA / TE were observed in 68.61%, 61.31%, 47.45%, 21.9%, and 19.71% respectively. All baseline characteristics of patients are summarized in Table 1.

Table 1 : Baseline Characteristics of the patients

Figures: n [column %] or Mean ± SD	Total (n = 137)	Gender		**p-value
		Male (n = 69)	Female (n = 68)	
Age	62.08 ± 10.91	63.46 ± 10.6	60.68 ± 11.12	0.135

Married	134 [97.81%]	68 [98.55%]	66 [97.06%]	0.55
CHF ≤ 40%	84 [61.31%]	52 [75.36%]	32 [47.06%]	<0.001*
Hypertension	94 [68.61%]	45 [65.22%]	49 [72.06%]	0.388
Diabetes	30 [21.9%]	16 [23.19%]	14 [20.59%]	0.712
Stroke / TIA /TE	27 [19.71%]	14 [20.29%]	13 [19.12%]	0.863
Vascular Disease	65 [47.45%]	39 [56.52%]	26 [38.24%]	0.032*
+Ischemic heart	63 [96.92%]	39 [100%]	24 [92.31%]	0.078
+Peripheral vascular	1 [1.54%]	0 [0%]	1 [3.85%]	0.217
+Any carotid or aortic	2 [3.08%]	0 [0%]	2 [7.69%]	0.078

***Statistically significant at 5% level of significance**
****P-values are based on z-test for proportions and t-test for mean**
+ Based on patients with vascular disease

CHA2DS2 VASc score is significantly higher in females as compare to male patients 3.75 ± 1.45 vs. 3.3 ± 1.15 with p-value = 0.048. Although no statistically significant gender difference is observed in distribution of CHA2DS2 VASc score. Majority of the patients were found to have CHA2DS2 VASc score in range of 2 to 4, CHA2DS2 VASc score of 5, 6, 7, and 8 was observed in 12.41%, 4.38%, 2.92%, and 0.73% respectively. Further details of the score in different gender is elaborated in table 2.

Table 2 : CHA_2DS_2 VASc score by gender

	Total (n = 137)	Gender		**p-value
		Male (n = 69)	Female (n = 68)	
CHA_2DS_2 VASc Score	3.53 ± 1.32	3.3 ± 1.15	3.75 ± 1.45	0.048*
CHA_2DS_2 VASc 2	33 [24.09%]	18 [26.09%]	15 [22.06%]	0.581
CHA_2DS_2 VASc 3	44 [32.12%]	27 [39.13%]	17 [25%]	0.076
CHA_2DS_2 VASc 4	32 [23.36%]	13 [18.84%]	19 [27.94%]	0.208
CHA_2DS_2 VASc 5	17 [12.41%]	8 [11.59%]	9 [13.24%]	0.77
CHA_2DS_2 VASc 6	6 [4.38%]	2 [2.9%]	4 [5.88%]	0.393
CHA_2DS_2 VASc 7	4 [2.92%]	1 [1.45%]	3 [4.41%]	0.303
CHA_2DS_2 VASc 8	1 [0.73%]	0 [0%]	1 [1.47%]	0.312
CHA_2DS_2 VASc 9	0 [0%]	0 [0%]	0 [0%]	-

*Statistically significant at 5% level of significance
**P-values are based on z-test for proportions and t-test for mean

Majority of our patients were taking Warfarin as an antithrombotic treatment while Rivaroxaban was prescribed to only 13.14% (18) patients. No statistically significant difference in antithrombotic treatment was observed by gender. Summary of antithrombotic and antiplatelet prescribed to different gender is presented in table 3.

Table 3 : Antithrombotic Treatment

	Total (n = 137)	Gender		**p-value
		Male (n = 69)	Female (n = 68)	
Antiplatelet	103 [75.18%]	58 [84.06%]	45 [66.18%]	0.185
Warfarin	86 [62.77%]	40 [57.97%]	46 [67.65%]	0.208
NOAC (Rivaroxaban)	18 [13.14%]	9 [13.04%]	9 [13.24%]	0.88

*Statistically significant at 5% level of significance
**P-values are based on z-test

Discussion

Our study showed majority of our patients 104 (75.91%) out of 137 were on anticoagulation which in comparison to a local study done by Ikramullah et al in which only 27.5% patients were taking anticoagulation[13], was encouraging as most of our patients are selected from dedicated Anticoagulant clinic, most of them 86 (62.77%) were on Warfarin and only 18 (13.14%) were taking Rivaroxaban. Recent guidelines are preferring use of Rivaroxaban over warfarin [14, 15] and this strategy is implemented although at a modest level in a number of countries[16]. In our study the number of patients on Rivaroxaban was very low probably because of the common documented barriers like concerns of bleeding[17] and some others reasons like cost to translate guidelines recommendations into clinical practice[18]. Our study population was small and patients were included from a tertiary care cardiac center so cant translate the real status of management of such patients in community where incidence and prevalence of AF is on rise with increasing age and hypertension[19,20].

Conclusion

Our study showed very small percentage of our AF patients with high risk of stroke were prescribed Rivaroxaban which is a very good alternative to conventional warfarin therapy in reducing stroke risk. It's important to propagate updated knowledge regarding NOACs use in our medical community and a large local trial can be done to ensure safety and efficacy in our local population to enhance confidence of treating Physicians.

Conflicts of Interests

None.

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