Research Article

Evaluation of thromboprophylaxis therapy in non-valvular atrial fibrillation Sudanese patients

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ABSTRACT

Background: Nonvalvular atrial fibrillation (NVAF) needs more carefully address, with special caution to the risk of ischemic stroke, which is the most serious complication. The first line of defense against NVAF related stroke is an anticoagulant. Anticoagulants have been used frequently for years to prevent and treat this potentially deadly blood clot. However, widely used traditional therapies are associated with significant limitations. **Objective:** Assessment and evaluation of current stroke prevention strategies and investigate whether the current used oral anticoagulant drugs have a major impact on stroke prevention in NVAF Sudanese patients. **Materials and Methods:** This was observational retrospective cohort study design, including 200 patients with diagnosed NVAF. The study was conducted in different Khartoum Cardiac centers. Patients with NVAF seen between 2013 and 2015 were identified in a database and followed up for mortality, stroke, and bleeding events. They were divided into two groups, 150 patient taking warfarin and 50 were on dabigatran (Pradaxa). This study included two patients' data collection forms which were prepared using specific measure tools of stroke and bleeding risk factors, CHA_2DS_2VASC score and [HAS-BLED] bleeding risk score, respectively. Patients with CHA_2DS_2VASC score <2 were excluded. **Results:** Among 150 NVAF patients taking warfarin, 48% of patients had stroke, 28% of patients had bleeding, and 2% passed away. Patients on 150 mg of dabigatran no stroke event or bleeding case were recorded. **Conclusions:** This study demonstrates that dabigatran is better than warfarin for NVAF Sudanese patients as an anticoagulation agent to prevent AF related stroke. It is associated with a decreased bleeding events and no significant increase in embolic events. Furthermore, it seems to have similar stroke prevention effect as well as warfarin.

KEY WORDS: Antithrombotic Drugs; Atrial Fibrillation; Warfarin, Arrhythmia; Pradaxa

INTRODUCTION

The world faces prevalence of atrial fibrillation (AF) and AF related stroke, which is the most common type of arrhythmia. During an arrhythmia, the heart can beat rapidly, slowly, or with an irregular rhythm. AF occurs if rapid, disorganized electrical signals cause the heart's atria to fibrillate. The term fibrillates means to contract very fast and irregularly.[1] In AF, if the atria blood is not pumped completely into the ventricles, the heart's upper and lower champers does not work together as they should. People with AF may be asymptomatic; however, even when AF is not noticed, it can increase the risk of stroke. In some people, AF can cause chest pain or heart failure, especially if the heartbeat is very fast.[1] Nonvalvular AF (NVAF) needs more carefully address, with special caution to the risk of ischemic stroke, which is the most serious complication. The first line of defense against NVAF related stroke is an anticoagulant. Anticoagulants have been used frequently for years to prevent and treat this potentially deadly blood clot. However, widely used traditional therapies

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are associated with significant limitations. The CHA_2DS_2-VASC stroke risk stratification scheme should be used as a simple initial (and easily remembered) means of assessing stroke risk.[2] On the other hand, assessment of bleeding risk should be part of the patient assessment before starting anticoagulation. Various bleeding risk scores have been validated for bleeding risk in anticoagulated patients, recently a new simple bleeding risk score; HAS-BLED has been derived.[3]

Objective

Assessment and evaluation of current stroke prevention strategies and investigate whether the current used oral anticoagulant drugs have a major impact on stroke prevention in NVAF Sudanese patients.

MATERIALS AND METHODS

This was observational retrospective cohort study design, including 200 patients with diagnosed NVAF. The study was conducted in different Khartoum Cardiac centers. Patients with NON AF seen between 2013 and 2015 were identified in a database and followed up for mortality, stroke, and bleeding events. They were divided into two groups, 150 patient taking warfarin and 50 were on dabigatran (Pradaxa). This study included two patients' data collection forms which were prepared using specific measure tools of stroke and bleeding risk factors, CHA_2DS_2VASC score and [HAS-BLED] bleeding risk score, respectively. Patients with CHA_2DS_2VASC score <2 were excluded.

Ethical Consideration

It is in the interests of both the institutions (study populations) and researcher that research projects are reviewed and conducted ethically, both to protect the rights and welfare of research subjects, as well as to enable international recognition for creditable institutional procedures. All patients' data were collected and reviewed after the approval of the hospital ethics committee. All participants were informed about the nature of the study and were informed that their participation in the study is voluntary, no names attached to the data collecting form. And assured that, the data provided will not be used in any way to support a decision, or harm against them.

Data Analysis and Statistics

The collected data were organized, tabulated, classified, and analyzed using statistical software program. Data entry and analyses took place once each data collection forms were reviewed for clarity and completeness using Statistical Package for the Social Sciences (SPSS) version 12.0. The results were further tabulated, interpreted, and discussed; figures were plotted using Microsoft Excel program (2007).

RESULTS

Patient's data were collected from different cardiac centers in Khartoum, and all patients with NVAF assessed for stroke risk using CHA_2DS_2VASC tool and bleeding risk using HAS-BLED tool. As illustrated in Figure 1, the result of Dabigatran patients' CHA_2DS_2VASC score and stroke rate was 22% of patients awarded 6 points, 20% awarded 5 points, 16% awarded 4 points, 14% awarded 3 points, 12% awarded 2 points, 8% awarded 7 points, and 8% awarded 8 points patients. Dabigatran patients' HAS-BLED bleeding risk score result was 42% of patients awarded 2 points, 30% awarded 1 point, 12% awarded 0 points, 8% awarded 7 points, 4% awarded 4 points, and 4% awarded 7 points. Figure 2 as shown in Figure 3 Warfarin patients' results, CHA_2DS_2VASC score results as follow 23% of patients awarded 2 points, 22% awarded 4 points, 14% awarded 5 points, 14% awarded 3 points, 10% awarded 6 points, 7% awarded 7 points, 6% awarded 9 points, and 4% awarded 8 points. Warfarin patients' (HAS-BLED bleeding risk score) results as follow 24% of patients awarded 1 point, 23% awarded 2 points, 18% awarded 5 points, 15% awarded 4 points, 11% awarded 3 points, and 9% awarded 0 points. As regards of patients, observational study Warfarin result was 72 patients had a stroke and was 3 passed away. Among all observational period of dabigatran (Pradaxa) in patients with NVAF no stroke event or bleeding case recorded as shown in Table 1.

DISCUSSION

This study mainly conducted to evaluate thromboprophylaxis therapy in NVAF Sudanese patients. Moreover, it was included 200 patients, 150 (75%) on Warfarin treatment and 50 (25%)

Table 1: Dabigatran versus warfarin in patients with risk event

Observational results	Number of patients	Bleeding risk	Number of passed patients	Stroke event
Warfarin patients	150	42	3	72
Dabigatran patients	50	0	0	0
Observational results	No of patient	Event rate with risk factor	Event rate without risk factor	Proportions
Warfarin patients	150	117	33	0.78
Dabigatran patients	50	0	50	0*

*Chi-square=93.96, $P<0.05$ significantly different

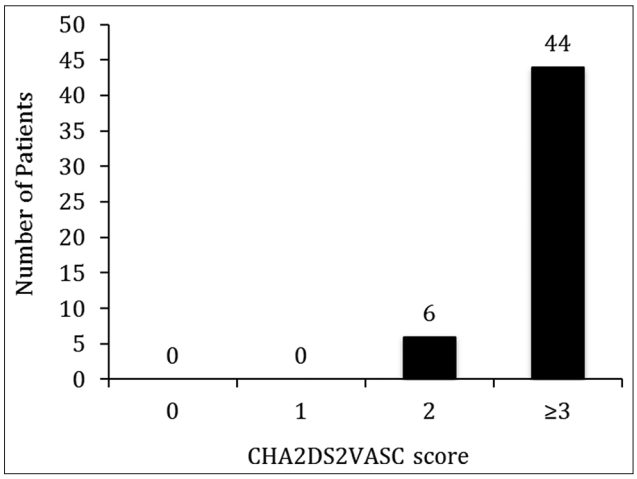

Figure 1: Illustration of dabigatran patients risk category according to CHA_2DS_2VASC score

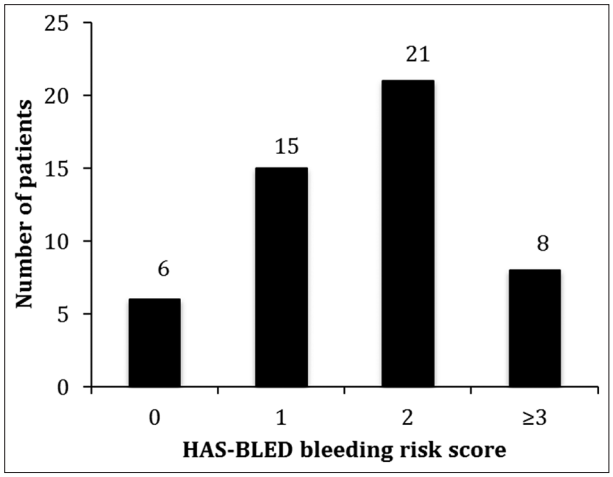

Figure 2: Demonstration of dabigatran patients risk category according to HAS-BLED bleeding risk score

on dabigatran. The two groups were balanced in terms of comorbidities. ($P = 0.00$ with significant difference) Predicted thromboembolic risk measured by the CHA_2DS_2-VASC score was similar between the groups. All patients have high risk for stroke and moderate to low risk for bleeding. During the study period, 48% of Warfarin patients had stroke 28% of patients had bleeding and 2% were passed away. While patients on dabigatran did not reported any stroke event and bleeding risk. This result is similar to result of study initiation of therapy with dabigatran which demonstrates that dabigatran is being adopted rapidly among Danish AF patients who are naïve to anticoagulant therapy.[4] Furthermore, meta-analysis demonstrates that novel oral anticoagulants (NOAC) are an alternative for AF anticoagulation and the result was that the 2614 patients on a NOAC (9.6% R) were similar to the 4262 patients on Warfarin. NOAC were stopped 2.5–96 h pre-procedure and restarted 1–48 h post-procedure; in 3190 (75%) Warfarin patients, Warfarin was uninterrupted. Composite bleeding rates were significantly lower in NOAC patients (4.47% vs. 6.96% in Warfarin, odd ratio (OR) 0.60, 95% confidence interval (CI) 0.48–0.75; I2 = 47%). Composite

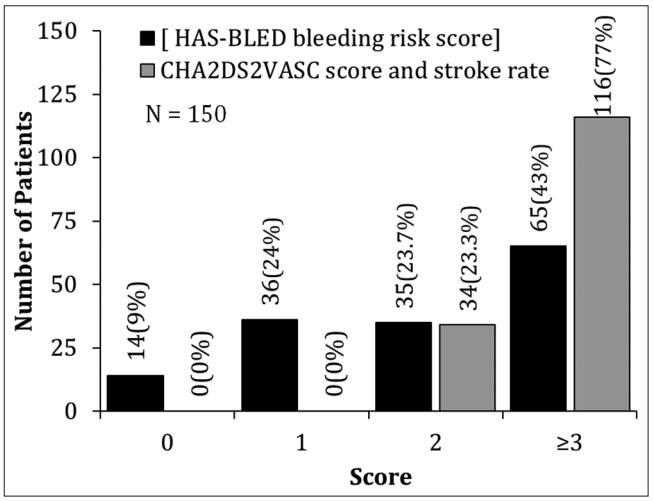

Figure 3: Distribution of Warfarin patients risk categories according to the CHA_2DS_2-VAScscore and HAS-BLED, respectively

embolic rates were similar in both groups (0.61% in NOAC vs. 0.39% in W, OR 1.42, 95% CI 0.76–2.66; I2 = 0%).[5] On the other hand, this study is in agreement with other studies were assigned randomly 113 patients who had AF and risk of stroke to receive in blinded fashion using fixed doses of dabigatran 110 mg or 150 mg twice daily or in adjusted dose Warfarin and the result in patients with AF dabigatran given at a dose of 110 is associated with rates of stroke and systemic embolism that were similar to those associated with Warfarin as well as lower rate of major hemorrhage. Dabigatran administrated at a dose 150 mg as compared with Warfarin was associated with lower rates of stroke and systemic embolism but similar rates of major hemorrhage.[6] Patients had seen between 2013 and 215, and they were assessed for both stroke risk and bleeding risk using CHA_2DS_2VASC score and HAS-BLED score, respectively, patients with CHA_2DS_2VASC score <2 were excluded. This finding is consistent with the royal college of physicians of Edinburgh which highlighted that all patients with AF should have a formal stroke risk assessment with a scoring tool such as CHA_2DS_2-VASC. It also states that the use of the HAS-BLED score can help identify modifiable bleeding risks that need to be addressed but emphasizes that it should not be used on its own to exclude patients from OAC therapy.[7] Considering all this we argue that using of Pradaxa will be more effective for Sudanese patients with NVAF, because of lacking of anticoagulant center and specialized cardiac hospital to providing them different type of consultation and international normalized ratio (INR) monitoring. In study was carried out in 967 centers in 44 countries within subgroup of patients with previous stroke or transient ischemic attack, 1195 patients were from the 110 mg dabigatran group, 1233 from the 150 mg dabigatran, and 1195 from the warfarin group. Stroke occurred in 65 patients on Warfarin compared with 55 on 110 mg dabigatran and 51 on 150 mg dabigatran the rate of major bleeding was significantly lower inpatient on dabigatran compared with those in warfarin.[8] Other study assigned to investigate the primary and secondary outcomes and the finding was the benefit of 150 dabigatran reducing

stroke, 110 mg at reducing bleeding, and both doses at reducing intracranial bleeding versus Warfarin advantages of dabigatran were greater at sites with poor INR control than at those with good INR control. Overall, these results show that the local standards of care affect the benefits of use of new treatment alternatives.[9] Other study was identified all AF patients initiating oral anticoagulation from August 2011 to December 2011. Patients with valvular AF, previous thromboembolism, or recent orthopedic surgery were excluded (n = 43). Temporal utilization trends were compared between initiators of Warfarin and dabigatran. Logistic regression analysis with backward selection was used to assess factors associated with initiation of dabigatran instead of Warfarin. Results show that dabigatran is being adopted rapidly among AF patients who are naïve to anticoagulant therapy.[10] Dabigatran compared with warfarin for stroke prevention with AF. Is other study was carried out in Hong Kong.[11] Furthermore, this study strongly agree with randomized study carried out to study safety, tolerability and the efficacy of idarucizumab for the reversal of the anticoagulation effect of dabigatran, results showed that idarucizumab was associated with a rapid and complete reversal and safe.[12] The powerful strength of this study was that achieved proof to use novel non-Vitamin K antagonist oral anticoagulants for patients with NVAF in Sudan as well as warfarin, especially for patients facing problems to monitor their INR lab result. Other strength addressed by the study was that, all patients in Sudan taking Warfarin for stroke prevention regardless of their tolerability, and if they will comply with their therapy regimen or not. One final strength achieved by this study was that, Pradaxa not widely used in Sudan and really most of the patients need to switch from warfarin therapy to Pradaxa.

Recommendations

This study strongly recommended that using of Pradaxa will be more effective for Sudanese patients with NVAF, because of lacking of anticoagulant center and specialized cardiac hospital to providing them different type of consultation and INR monitoring.

CONCLUSION

This study demonstrates that dabigatran is better than Warfarin for NVAF Sudanese patients as anticoagulation agent to prevent AF related stroke. It is associated with a decreased bleeding events and no significant increase in embolic events. Furthermore, it seems to have similar stroke prevention effect as Warfarin as well.

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