

ASSESSMENT OF ANTICOAGULANT DRUGS IN ELIGIBLE PATIENTS WITH ATRIAL FIBRILLATION

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ABSTRACT

Background

Atrial fibrillation is associated with substantial mortality and morbidity from stroke and thromboembolism. Despite an efficacious oral anticoagulation, atrial fibrillation patients at high risk for stroke are often under-treated.

Objectives

To detect the percentage of anticoagulant eligible patients with atrial fibrillation not receiving anticoagulant therapy and its causes, and whether the INR target is reached or not.

Materials and Methods

A cross-sectional study in the medical emergency department and neurology unit of Shar hospital in Slemani city was carried out, from the 1st of Jan 2017 to the 1st of Dec 2017, on a sample of two hundred and seventy-two patients with atrial fibrillation. Data were obtained from the patient's case notes for their personal detail including age, sex, history of hypertension, diabetes mellitus, vascular disease, heart failure, and thromboembolism.

Results

Two hundred seventy-two patients diagnosed with atrial Atrial Fibrillation, 148 (54.4%) females 124 (45.6%) males, mean age 70.43 years were analyzed and among these patients, 24 had valvular AF and 248 had no valvular AF patients. Warfarin was prescribed in 54(19.85%), antiplatelet in 63 (23.16%) patients, new oral anticoagulant in 19 (6.98%) patients and no antithrombotic therapy in 136 (50%) patients. The common cause behind why most patients with AF were not prescribed anticoagulants was; not prescribed by a physician 107 (53.76%) patients. Regarding those patients prescribed warfarin only 26 (48.1) patients INR level was in the therapeutic range.

Conclusion

This study demonstrates underuse of oral anticoagulation therapy for atrial fibrillation patients with high risk of stroke.

Keywords: *Atrial Fibrillation, Oral anticoagulant, INR.*

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INTRODUCTION

Atrial fibrillation (AF) is the most common sustained cardiac rhythm disorder, affecting 1% to 2% of the general population ⁽¹⁾. Its incidence increases dramatically with age, from less than 0.5% at 40 to 50 years, to 10% in octogenarians ⁽²⁾. The risk of stroke is approximately 5 times higher in patients with AF ⁽³⁾. The CHADS2 score has been available and validated for stroke risk stratification for the past decade, and was cited by national treatment guidelines as a tool to determine when oral anticoagulation is warranted, it remains unclear to what extent it has been routinely used in clinical practice to guide decisions on anticoagulation therapy ⁽⁴⁾. It has been suggested that the CHADS2 score may not be sensitive in stratifying patients clearly into low-, intermediate-, and high-risk groups in clinical practice ⁽⁴⁾. The more recently developed stroke stratification scheme, CHA2DS2-VASc ⁽⁵⁾, Oral anticoagulants (OACs) are more effective than aspirin in reducing the stroke risk but are also associated with an increased bleeding risk. Therefore, anticoagulant recommendations depend upon balancing the expected benefit of stroke risk reduction against the increased harm from bleeding in patients with different factors that are prognostic for strokes and bleeding ⁽⁶⁾. Warfarin, a vitamin K antagonist, is routinely used for anticoagulation and is effective in reducing stroke and death risk in patients with Non-Valvular AF ⁽⁷⁾. Despite possessing a number of limitations ⁽⁸⁾, including food and drug interactions, the need for close laboratory monitoring to ensure the prothrombin time–international normalized ratio (PT-INR) is maintained within a narrow therapeutic range, and a high risk of bleeding when the high end of this range is exceeded, warfarin has been used extensively for patients with NVAF in clinical practice ⁽⁹⁾. In comparison to NOACs, anticoagulant monitoring for warfarin is validated, an antidote is available for toxicity and long-term safety is well established. Recently, non–vitamin K-dependent, oral anticoagulants (DOACs; dabigatran, rivaroxaban, apixaban, and edoxaban) have become available for the prevention of stroke and systemic embolism in patients with NVAF. Newer oral anticoagulants (NOACs) have some limitations like lack of antidote, unknown long-term safety and lack of validated tests to monitor anticoagulant effect [27] Although the risk of major bleeding remains, DOACs offer an improved risk benefit profile (e.g., less risk of intracranial bleeding) compared with warfarin. Of note, though, risk profiles also differ among DOACs ⁽¹⁰⁻¹²⁾. Compared with

warfarin, DOACs have a more rapid onset ⁽¹³⁾; shorter half-lives, which can aid timing of surgery ^(13, 14); fewer drug and food interactions [15]; no need for routine laboratory monitoring [13]; and potential for fixed dosing ⁽¹⁵⁾. JCS guidelines also recommended PT-INR targets of 2.0-3.0 in warfarin-treated patients younger than 70 years and 1.6-2.6 for those aged 70 years and older ⁽¹⁶⁾.

PATIENTS AND METHODS

A cross-sectional study was carried out for a period of eleven months, from first Jan 2017 to 01 Dec 2017. The data were obtained from the admitted patients (with atrial fibrillation) case sheet of their personal detail, through direct questionnaire, full detailed history we calculated the CHA2DS2-VAS score by adding 1 point for the following condition; congestive heart failure, hypertension, diabetes, age between 65-75 years, vascular disease, sex category (female), and 2 points for age above 75 years and history of stroke or TIA. The patients were assessed by history and physical examination for anticoagulant drugs, side effects, and their compliance, Also for the complication of AF. Electrocardiography and echocardiography were done for all patients, PT, PTT, INR was done for patients on warfarin. Patients were excluded if they had a CHA2DS2-VAS score = 0 or 1 and reversible causes of AF (cardiac surgery, hyperthyroidism, pregnancy, pneumonia.). The patients were also assessed why they are not on anticoagulation drugs.

Data analysis was done by computerized statistical software; statistical package for social sciences (SPSS) version 22. Descriptive statistics were presented as (mean±standard deviation) and frequency as percentages. In all statistical analysis, the level of significance (p-value) was set at < 0.05.

RESULTS

In this study a Total of 272 patients with AF patients were included, 148 (54.4%) females 124(45.6%) males, the mean age of the participants was 70.43±9.80 years. Twenty four (8.82%) patients were valvular AF and two hundred eight (91.17%) were Non-valvular AF.

All patients had CHA2DS-VASc score ≥ 2. Of these, 136 patients (50%) who were eligible for anticoagulation had not been prescribed appropriate anticoagulant therapy, 54 (19.85%) patients were prescribed warfarin, 19(6.98%) patients new oral anticoagulants (rivaroxaban or dabigatran) and 63 (23.16%) patients had antiplatelet,

Assessment of Anticoagulant Drugs in Eligible Patients with Atrial Fibrillation

details of antithrombotic drugs prescribed are shown in Table 1.

Analysis of the causes of inadequate or improper utilization of guideline-directed therapy revealed that; 107 patients (53.76%) patients were not offered anticoagulation by the physician, 35(17.58%) patients were due to patients' non-adherence, 18(9.04%)patients due to side effects and in 39 patients (19.59%) because of cost and difficult follow up. Details of these factors

are shown in Table 2.

Regarding INR target for patients on warfarin, Only 26 patients (48.1%) had an INR level within target, while 12 patients (22.2%) had INR level of less than 2, 14 (25.9%) patients above 3 and 2 (3.7%) patients not monitored these figures are shown in Table 3.

Distribution and types of embolic complication are shown in Table 4

Table 1. Anticoagulant and antiplatelet medications in AF patients (n)%.

Drug	N (%)
No anticoagulant	136 (50%)
Warfarin	54 (19.85%)
Antiplatelets	63 (23.16%)
New oral anticoagulants	19 (6.98%)
Total	272 (100%)

Table 2. Factors contributed to lack of appropriate anticoagulation.

Causes of not prescribing anticoagulants	N(%)
Not prescribed by the physician	107 (53.76%)
Non-adherence	35 (17.58%)
Drug side effects	18 (9.04%)
Cost and difficult follow up	39 (19.59%)
Total	199 (100%)

Table 3. INR Target in those receiving warfarin.

INR	WARFARIN (N) & %
Less than 2	12 (22.2%)
INR between 2-3	26 (48.1%)
INR above 3	14 (25.9%)
No monitoring	2 (3.7%)
Total	54 (100%)

Table 4. Occurrence of embolic complication among patients with and without treatment.

Embolic Complication	With treatment (N)	Without treatment (N)	P value
None	97 (71.32)	64 (47.05)	0.001
CNS EMBOLI	36 (26.47)	59 (43.38)	
WISEARAL EMBOLI	1 (0.73)	8 (5.88)	
EMBOLI IN EXTREMITIES	2 (1.47)	5 (3.67)	
Total	136 (100%)	136 (100%)	

DISCUSSION

In this study, we assessed the rate of appropriate anticoagulant drug usage among eligible patients with AF as recommended per guidelines both in patients with valvular and non-valvular AF. Out of 272 cases with AF, all had the CHA2DS2-VASc score equal to or higher than 2. Females patients were higher in number (54.4%). This is consistent with another study conducted in India by Patel DS et al which showed higher rates of females with AF (58% were female and 42% male)⁽¹⁷⁾. Reason for this gender difference could be due to higher rates of rheumatic heart disease in females.⁽¹⁸⁾, in another study by Ewen E et al which showed higher rates of males with AF (48.3% were female and 51.7% male)⁽¹⁹⁾.

In this study the patients mean age was 70.43±9.80 years. However, in other studies, the mean age was 60–80 years^(20–22). This study showed that patients taking warfarin had a lower relative risk of embolic complication by 24.26% than those who did not take warfarin. Using a similar methodology, Lakshminarayan and colleagues reported a 26% lower risk of ischemic stroke in patients with NVAf taking warfarin. [33] In our study Anticoagulants were prescribed for 73 patients (26.83%). This differed from a study conducted in the United States by Ewen E et al which showed that 67% of patients were prescribed anticoagulant⁽¹⁹⁾. However, two other studies Ceresne L et al and Smoyer-Tomic K et al showed that the extent of use of anticoagulant was 76–79%^(23, 24).

This study showed that antiplatelets were prescribed for 63 patient (23.16%), this result was different from other studies done in united states and China, (45.9% and 73.4%) respectively^(25, 26). This shows the use of antiplatelet and anticoagulant drugs in AF patients is highly variable even in developed countries. In this study, 136 (50%) AF patients out of total 272 AF

patients were not prescribed antithrombotic therapy. However, a study by Burgess C et al⁽²⁸⁾ among 150 known AF patients, 54 (36%) patients were not on any antithrombotic treatment.

In this study out of 272 AF patients, 54 (19.85%) patients were prescribed warfarin, 19 (6.98%) new oral anticoagulant, 63 (23.16%) antiplatelet and no antithrombotic therapy in 50% patients. In accordance to this; a study by Leung CS et al⁽²⁹⁾ conducted among 207 patients in Hong Kong showed that 44% NVAf patients were receiving warfarin, 34.1% aspirin and 22% no antithrombotic therapy.

In this study reason for not prescribing antithrombotic drugs in 272 eligible AF patients were; [not prescribed by physician in 107 (53.76%) patient, 35 (17.58%) patients non-adherence, 18 (9.04%) patients stop drug due to side effects and in 39 (19.59) patients because of cost and difficult follow up. There are several reasons that may explain the lack of adherence to treatment guidelines observed in this analysis, including difficulties in extrapolating clinical trial data to patients who may have a complex medical history; lack of awareness; lack of opportunity to evaluate and adopt guidelines to local clinical practice; cultural barriers; psychological factors (e.g. physician fear of bleeding/intracranial haemorrhage); and economic issues (which are particularly apparent in developing countries, where there can be barriers to physicians prescribing effective treatments or accessing monitoring tests⁽³⁰⁾.

The lack of international normalized ratio (INR) monitoring in outpatient clinics in some countries or regions and contraindications to OAC use in some patients might also explain the non-adherence to guidelines⁽³¹⁾.

In this study of 272 eligible AF patients, 54 patients were prescribed warfarin and 26 (48.1) patients INR

level were within the target therapeutic range (2-3), 26(48.1%) patients were not within therapeutic range and 2(3.7%) patients not monitored. In another study out of 620 patients, the majority of patients (63.2%; n = 392) were not within the target therapeutic range for AF⁽³²⁾. Moreover, this may explain the difficulty of managing patients on anticoagulant treatment. It is important to monitor anticoagulation status but it is not possible for all patients due to higher cost, need for frequent monitoring and dose adjustments. those patients admitted to hospital with a stroke while receiving warfarin therapy, most have subtherapeutic international normalized ratios^(34, 35).

In conclusion, this study demonstrates underuse of oral anticoagulation therapy for atrial fibrillation patients with high risk of stroke.

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