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Prevailing Practices of Usage of Oral Anticoagulant in Stroke Prevention in Atrial Fibrillation (SPAF) in Indian Patients: Results of a Multicenter, Cross Sectional Questionnaire Based Physician Survey

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Authors' contributions

This work was carried out in collaboration between both authors. Authors AS and VR were involved in all aspects such as conceptualization, definition of intellectual content, literature search, data acquisition and analysis, manuscript editing, review and approved the final version of the manuscript for publication.

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ABSTRACT

Objective: Understanding physician's opinion on usage and challenges for use of oral anticoagulants (OACs) in SPAF (Stroke Prevention in Atrial Fibrillation).
Materials and Methods: A multicenter questionnaire based survey was conducted among Indian physicians. Questionnaire included items related to number of patients with atrial fibrillation (AF) seen, use of different scoring systems, international normalized ratio (INR) monitoring, issues preventing prescription of OAC, perceived concerns while using vitamin K antagonists (VKA) in SPAF.
Results: Ninety-three physicians participated. Mean number of AF patients seen by doctors per month was 28.05(60.02). Seventy-two (77.4%) and 47(50.5%) physicians reported using "CHA 2

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DS 2-VASc" and the "HAS BLED score" respectively. Routine use of VKA and aspirin was reported by 71(76.3%) and 60(64.5%) physicians respectively. Thirty-one (33.3%) physician reported INR monitoring twice per week at the time of diagnosis until patient is stabilized within therapeutic range. During dosage adjustment, INR monitoring is performed twice a month by 38(40.9%) physicians. When the patient is stable on treatment, 47(50.5%) reported monitoring 3-6 times per year. Low diagnosis rate, difficulty of monitoring, low patient awareness and cost are the important limitations for use of OAC for SPAF. Inconvenience and burden of INR monitoring is an important/very important perceived issue by the patients for use of anti-coagulants in SPAF according to 89(95.7%) physicians. Seventy-six (81.7%) doctors reported that dose adjustment is very important/important challenge while using VKA in SPAF.

Conclusion: Burden of atrial fibrillation is high in India. Use of CHA 2 DS 2-VASc is common among Indian physicians. About two third physicians use VKA for SPAF. Poor diagnosis rate, difficulty of monitoring, low patient awareness and cost are the major limitations for using OAC for SPAF.

Keywords: INR; monitoring; oral anticoagulants; stroke prevention in atrial fibrillation.

1. INTRODUCTION

Atrial fibrillation is the most common and clinically significant type of cardiac arrhythmia worldwide [1]. Incidence of atrial fibrillation is rising [2]. There is very limited epidemiological data on atrial fibrillation in India [3,4]. Increased risk of ischemic stroke and heart failure [1,5] and higher mortality and disability associated with atrial fibrillation related strokes compared to those without it, [6] necessitates prompt treatment of atrial fibrillation. Atrial fibrillation is an important cause of cardioembolic cerebral infarction and also a predictor of increased mortality in patients with cerebral infarction [7]. Anticoagulation therapy is required in patients with atrial fibrillation to prevent stroke and reduce risk of systemic embolism [8,9]. Due to risk of stroke, antithrombotic therapy is recommended to all patients with atrial fibrillation except those with low risk of stroke [6].

Over the years, especially in last decade there has been significant evolution of understanding and usage oral anticoagulants for stroke prevention in patients with atrial fibrillation (SPAF) [4]. Several anticoagulants including vitamin K antagonists (VKA), ie acenocoumarol and warfarin and newer oral anticoagulants (NOAC) such as dabigatran, apixaban and rivaroxaban are currently available for SPAF [10-12]. There is no clarity on the comparative effectiveness and safety of different anticoagulants used in routine practice especially in the Indian population. International guidelines [13] and Indian consensus [4] are available for SPAF. However, global data suggest poor adherence to guidelines for SPAF [14,15]. A retrospective study from a tertiary hospital showed only 38.7% patients with CHADS2 >2 were discharged with anticoagulant whereas remaining 61.3% were not prescribed anticoagulants [15]. Moreover, there might be differences in recommendations and real life clinical practice [16,17]. Understanding patients' preferences and partnering with them in decision making process is important while choosing therapy for SPAF [18]. Understanding the real life clinical practice approach and challenges for using anti-coagulant in SPAF may be useful in forming, refining guidelines or evaluating practicality of recommendations in Indian setting. Research on physician perceptions about use of VKA oral anticoagulants for stroke prevention is limited.

This study was conducted to understand physician's opinion regarding common presentation of atrial fibrillation, different scoring systems for prediction of risk of stroke and usage and challenges for use of oral anticoagulants in SPAF.

2. MATERIALS AND METHODS

A multicenter, cross sectional questionnaire based survey was conducted among Indian physicians. The criterion for enrolling physicians in the survey was experience of using oral anticoagulants for treating for SPAF. Enrolled physicians were contacted in person and subjected to detailed pre-formed questionnaire on atrial fibrillation and usage of anticoagulants in prevention of stroke. The questionnaire included items related to number of patients with atrial fibrillation seen per month, distribution of valvular and non-valvular AF, use of "CHA2DS 2-VASc" score system as a clinical prediction rule for estimating the risk of stroke, "HAS BLED score" (if not used, then reasons for it), approach

towards management of SPAF (choice of anticoagulant and sequence of its usage), frequency of international normalized ratio (INR) monitoring (when patient is on anticoagulant treatment at the time of diagnosis, during dosage adjustment and on stable treatment), main issues preventing patients with atrial fibrillation being prescribed an oral anticoagulant regimen for stroke prevention, main perceived issues by patients with the use of anti-coagulants in SPAF and common challenges of physicians while using VKA in SPAF. Experience of using oral anticoagulants in all types valvular diseases (irrespective or severity) was recorded. Survey participants were requested to rank main issues preventing AF patients being prescribed an oral anticoagulant regimen for stroke prevention on the scale of 1 to 4 (1-most important; 4-least important). The main perceived issues by patients with the use of anti-coagulants in SPAF and challenges of physicians while using VKA in SPAF were ranked as very important, important, neither important nor non-important and non-important.

Standard descriptive statistics was calculated for all the non-missing data. Qualitative data is described using standard descriptive statistics, counts (n), and percentages (%). Standard descriptive statistics for quantitative data include mean and standard deviation (±SD).

3. RESULTS AND DISCUSSION

A total of 93 physicians were participated in this study. The mean number of patients with atrial fibrillation seen by these doctors per month was 28.05(±60.02). The number (%) of doctors treating 1-20, 21-100 and 101-400 patients per month were 73(78.5%), 14(15.1%) and 5(5.4%) respectively.

The distribution of valvular and non-valvular atrial fibrillation in clinical practice is 47.5% and 53.2% respectively.

A total of 72 (77.4%) physicians reported that they use “CHA 2 DS 2-VASc” score system as a clinical prediction rule for estimating the risk of stroke in patients while 21(22.6%) reported that they do not use it. The reasons for not using it included not being aware of it 7(7.5%), difficult to remember 5(5.4%), not being accurate 2(2.2%), not aware and difficult to remember 1(1.1%) and other reason 4(4.3%).

A total of 47 (50.5%) physicians reported that they use the “HAS BLED score” while 45(48.4%) reported that they do not use it. The reasons for not using “HAS BLED score” included not being aware of it 23(24.7%), difficult to remember 12(12.9%), not accurate 2(2.2%) and other reasons 7(7.5%).

Routine use of VKA and aspirin was reported by 71(76.3%) and 60(64.5%) physicians respectively. VKA and aspirin were reported to be used as first line agents by 47(50.5%) and 24(25.8%) physicians respectively. Newer oral anticoagulants, heparin and fractioned heparin are routinely used by 29(31.2%), 32(34.4%) and 32(34.4%) physicians respectively. Reported use of other agents and sequencing in the management of SPAF is shown in Table 1.

Table 1. Approach for stroke prevention in atrial fibrillation management

	VKA N(%)	Aspirin N(%)	NOAC (Newer oral anticoagulation) N(%)	Clopidogrel N(%)	Clopidogrel, atorvastatin N(%)	Heparin N(%)	Fractionated heparin N(%)
Yes	71 (76.3)	60 (64.5)	29 (31.2)	3 (3.2)	1 (1.1)	32 (34.4)	32 (34.4)
No	1 (1.1)	11 (11.8)	16 (17.2)	0 (0.0)	0 (0.0)	12 (12.9)	14 (15.1)
First line	47 (50.5)	24 (25.8)	9 (9.7)	1 (1.1)	1 (1.1)	16 (17.2)	11 (11.8)
Second line	5 (5.4)	18 (19.4)	18 (19.4)	1 (1.1)	0 (0.0)	5 (5.4)	9 (9.7)
First/second line	--	1 (1.1)	--	--	--	1 (1.1)	--

3.1 Frequency of INR Monitoring When Patient is on Anticoagulant Treatment Regimen

A total of 31(33.3%) physician reported that they monitor INR twice per week at the time of diagnosis until patient is stabilized within therapeutic range whereas 17(18.3%) physicians reported monitoring it once and thrice per week each. When the patient requires dosage adjustment, INR monitoring is performed twice a month by 38(40.9%) physicians and once a month by 16(17.2%) physicians. A total of 13 (14%) physicians reported monitoring thrice in a month. When the patient is stable on treatment, 47(50.5%) reported monitoring of INR 3-6 times per year.

Low diagnosis rate, difficulty and cost of monitoring, low patient awareness (non-symptomatic illness) and treatment cost were reported as the most important factor preventing AF patients being prescribed an oral anticoagulant regimen for stroke prevention according to 25(26.9%), 29(31.2%), 32(34.4%) and 27(29%) survey participants respectively. Seven (7.53%) physicians reported that other factors are most important.

3.2 Main Perceived Issues by Patients, Associated with the Use of Anti-coagulants in SPAF

Inconvenience and burden of INR monitoring is an important/very important perceived issue by the patients for use of anti-coagulants in SPAF according to 89(95.7%) physicians participated in survey. Need of dose adjustment is an important/very important perceived issue as per the opinion of 76(81.7%) physicians. A total of 74(79.6%) reported that perceived risk of bleeding is an important/very important issue for the patients while using anti-coagulants in SPAF. Drug and dietary interactions are important/very important issue for the patients according to 68(73.1%) physicians. Cost of therapy was reported as important/very important issue for patients by 54(58.1%) physicians whereas according to 20(21.5%) and 13(14%) physicians it is neither important nor non-important or un-important issue respectively (Fig. 1).

3.3 Common Challenges of Physicians While Using VKA in SPAF

A total of 76(81.7%) doctors reported that need of dose adjustment is very important/important challenge while using VKA in SPAF. Perceived risk of bleeding is very important/important challenge according to 85(91.4%) physicians. A total of 70(75.27%) physician consider drug and dietary interactions as a very important/important challenge. Patient compliance was reported as very important/important challenge by 84 (90.3%) physicians. According to 83(89.2%) physicians, patient follow up is important/very important challenge while using VKA in SPAF. Seventy-nine (85%) physicians reported inconvenience and burden of INR monitoring as important/very important challenge (Fig. 2).

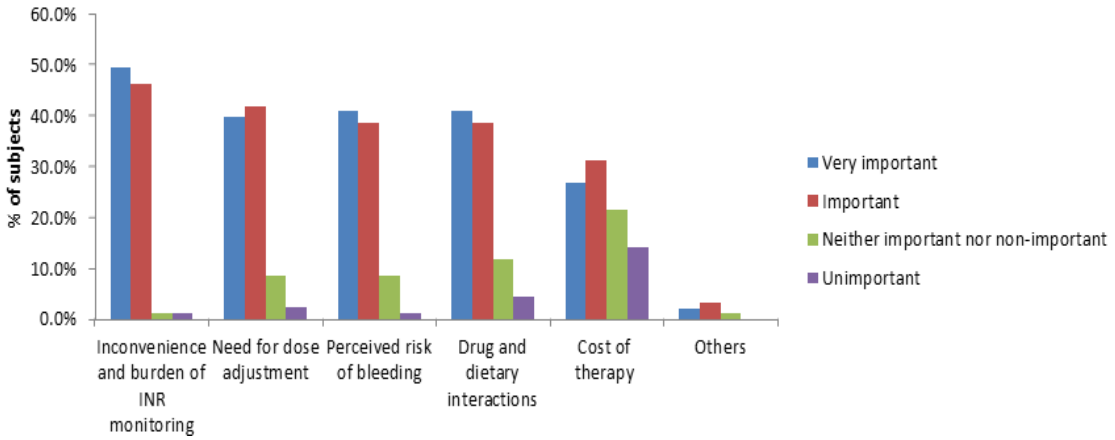

Fig. 1. Main perceived issues by patients with the use of anti-coagulants in stroke prevention in atrial fibrillation

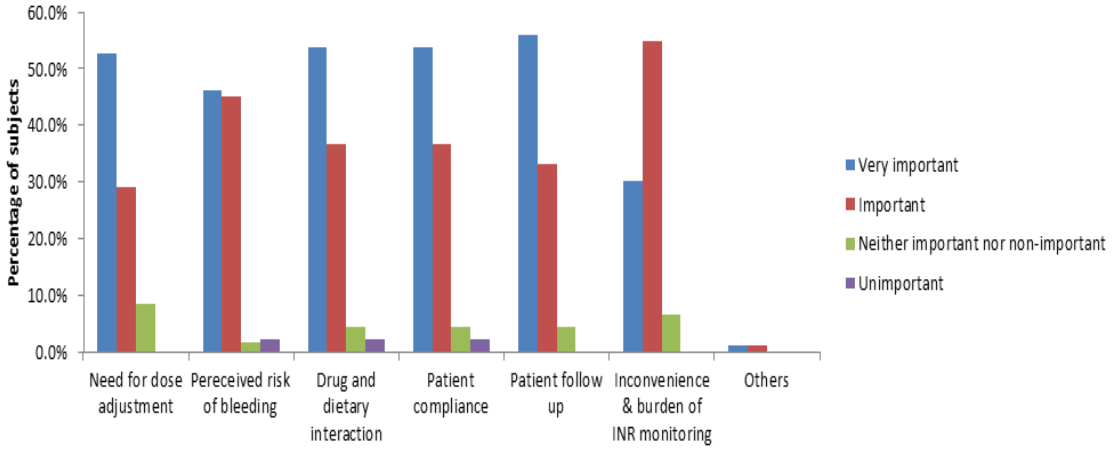

Fig. 2. Common challenges a physician faces while using VKA in stroke prevention in atrial fibrillation

Atrial fibrillation, a common type of cardiac arrhythmia is a known risk factor for stroke [6]. In this survey, we evaluated common presentations of atrial fibrillation in Indian patients and management pattern of SPAF including use of different scores for prediction of risk of stroke and bleeding and usage and challenges for use of oral anticoagulants in SPAF. We observed high burden of atrial fibrillation in India as indicated by large number of patients with atrial fibrillation seen by survey participants. Epidemiological data on atrial fibrillation in India is limited. Similarly, the exact prevalence of valvular versus non-valvular atrial fibrillation in Indian patients is not known. In our study, we did not find considerable difference in the prevalence between two types (47.5% versus 53.2%). Burden of valvular atrial fibrillation consists of patients with mechanical heart valves and rheumatic mitral stenosis [4].

European Primary Care Cardiovascular Society (EPCCS) consensus guideline on SPAF recommends CHA2DS2-VASc score for assessment of stroke risk [13]. We observed that more than three quarters survey participants use “CHA 2 DS 2-VASc” score system as a clinical prediction rule for estimating the risk of stroke. Those who do not use are either not aware of it, find it difficult to remember or have belief that the score is not accurate. There is no data on utility and accuracy of this scoring system in Indian patients. Further studies might be useful to estimate its usefulness in real life practice. However, only 50% of the participants used HAS-BLED score before prescribing anticoagulants.

Oral anticoagulant therapy is the choice of treatment for stroke prevention in patients with atrial fibrillation [19]. The European guideline recommends that all patients with atrial fibrillation having high risk of stroke, should be offered treatment with anticoagulants [13]. The landmark trial, Stroke Prevention in Atrial Fibrillation Study published in 1991 showed that aspirin and warfarin are both effective in decreasing risk of ischemic stroke in patients with atrial fibrillation [5]. All major trials have compared Non-vitamin K antagonist oral anticoagulants (NOACs) versus warfarin. However, other VKAs like acenocoumarol are also commonly used in patients with atrial fibrillation [20].

The Global Registry on Long-Term Oral Antithrombotic Treatment in Patients with Atrial Fibrillation (GLORIA-AF), a global registry in patients with newly diagnosed non-valvular atrial fibrillation at risk of stroke reported use of oral anticoagulants in 79.9% patients. A total of 47.6% received NOAC and 32.3% VKA; 12.1% received antiplatelet agents; 7.8% received no antithrombotic treatment [11]. In newly diagnosed non-valvular atrial fibrillation patients, use of NOAC is common than VKA in Europe and North America [12]. Our observations were different. In our study, routine use of VKA was reported by 76.3% participants. In terms of sequencing, VKA was reported to be used as first line agents more commonly than aspirin. In the large PINNACLE registry, antiplatelet agents were more common in paroxysmal compared to persistent atrial fibrillation [21]. However, in our study, aspirin was used as first line agent by 25.8% of the physicians for SPAF. Despite anticoagulants

being clearly indicated in these patients, first line use of aspirin is surprising. Physician's confidence in using anticoagulants in patients receiving aspirin will ensure passing benefits of anticoagulants to these patients. In our study, number of participants routinely using newer oral coagulants was lower compared to those using VKAs. The lower rates of use of NOACs could be because of higher cost. We observed good acceptance of oral anti-coagulants in Indian physicians for SPAF. Oral anticoagulants are under-prescribed for prevention of stroke in elderly patients with atrial fibrillation [19]. We did not evaluate the practice of using oral anticoagulants in this population. Worldwide, VKAs such as warfarin or acenocoumarol have been used for SPAF for long time. Even today, Acenocoumarol is widely used in Mexico, Latin American countries, and Spain [6]. Similarly, in India, use of VKA is common, according to the results of our survey. A Spanish study reported rise in oral anti-coagulants use in patients with atrial fibrillation mainly contributed by the use of NOAC [22]. In a recent study, NOACs was shown to be associated with a higher risk of gastrointestinal bleeding. Efficacy of NOACs and VKAs are similar in prevention of stroke whereas aspirin was not effective in SPAF [12]. A study from Poland reported more common use of antithrombotic therapy in patients with valvular atrial fibrillation compared to non-valvular AF [23]. We did not compare the use of antithrombotic therapy between two groups. Further studies may be required to confirm the pattern of antithrombotic drug usage in these two types of atrial fibrillation in Indian patients.

Anticoagulant therapy is associated with risk of bleeding; hence risk stratification of bleeding is important [9]. The EPCCS guideline suggests that HAS-BLED score may be considered to find out modifiable risk factors to reduce the risk of bleeding [13]. In our study almost half of the survey participants reported using it. Those who do not use it, cited similar reasons as for usingCHA2DS2-VASc score, but the number of respondents citing these reasons were different. Wider awareness and use of the HAS-BLED score may improve the confidence of physicians regarding their apprehension of bleeding with the use of oral anticoagulants.

The rates of INR monitoring were different at the time of diagnosis (i.e. after initiation of anticoagulant treatment till stabilization of patient), during dosage adjustment and during stable dosing. The rate of monitoring is reduced in sequential manner during these situations with intensive monitoring during initiation of anticoagulant.

Large number of patients particularly from Asia and North America are undertreated [10]. Unaffordability of oral anticoagulants is one of the common reasons for less common use of oral anticoagulants in patients with atrial fibrillation. The other reasons include physician inertia to initiate oral anticoagulants therapy, and poor understanding of importance of adherence [1]. We asked survey participants about the limiting factors for use oral anticoagulants for SPAF in India. The reasons cited by survey participants included low diagnosis rate, difficulty and cost of monitoring, low patient awareness and treatment cost. Inconvenience and burden of INR monitoring, need of dose adjustment, perceived risk of bleeding and drug and dietary interactions are considered important factors while using oral anticoagulants.

Guideline recommends that patient preferences should be considered in deciding need and type of anticoagulation therapy [5]. Treatment related side effects, [20,24] risk of stroke, availability of measure to assess the effect of medicine, and availability of an antidote [25] and cost [26] are the important factor for selection of oral anticoagulants for SPAF.

Our study has some limitations. Convenience sampling method, small sample size and cross sectional study design limits the generalization of observations of this survey. Nevertheless, our study provides significant insights on the use and challenges for prescribing oral anticoagulants for SPAF.

4. CONCLUSION

Burden of atrial fibrillation is high in India. Use of CHA_2 DS_2-VASc for stroke risk prediction is common among Indian physicians. Despite availability of NOACs, close to two third physicians still use VKA for SPAF. Poor diagnosis rate, difficulty of monitoring, low patient awareness and cost (diagnosis and treatment related) are the major limiting factors for using oral anticoagulants for SPAF.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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