Cross-sectional Survey of Anticoagulant Use among Specialist Physicians with a Focus on Direct Anticoagulants

Abstract

Introduction: Direct oral anticoagulants (DOACs) have been available for clinical use since 2010 and offer the advantages of a lower bleeding risk with similar efficacy compared to Vitamin K antagonists (VKAs). However, no data is available on practice patterns anticoagulation usage and determinants of the same among physicians in India. **Methods:** A cross-sectional survey was conducted using Google Forms comprising of 24 questions in 4 categories on baseline information, practice details, knowledge, and outlook. **Results:** A total of 412 physicians were contacted, of which complete responses were received from 50 (12%). Majority had a subspecialist (58%) or a specialist (32%) qualification, with 54% working in a medical college. VKAs were the preferred first-line agent for 46%, with the most common perceived disadvantage being need of regular monitoring. The absence of regular blood testing was the most prominent advantage attributed to novel oral anticoagulants (NOACs) by 76% participants. Equivalent number of participants perceived efficacy to be similar in both groups, and 86% indicated NOACs to have better safety. Most participants responded to knowledge-based questions correctly and cited high costs of DOACs as the most common barrier to clinical use (78%). **Conclusions:** Our survey indicates VKAs as the preferred first-line agents despite perceived disadvantages. Among specialist physicians, high drug costs and not lack of knowledge or familiarity appear to be predominant factors precluding more frequent use of NOACs.

Keywords: *Acitrom, bleeding, novel oral anticoagulant, thrombosis, warfarin*

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Introduction

Oral anticoagulants are the mainstay of treatment for the prevention of recurrent venous thromboembolism (VTE) and ischemic stroke in atrial fibrillation.[1] VTE includes deep venous thrombosis (DVT) and pulmonary embolism (PE) and constitutes a significant global health-care burden, with an estimated incidence of 115–269 and mortality of 9–32 per 100,000 population.[2] A similar burden is imposed by atrial fibrillation, with an estimated 33 million patients worldwide as of 2010, which is expected to be much higher at present.[3] Before directly acting oral anticoagulants (DOACs) were introduced in 2010, Vitamin K antagonists (VKAs) were only oral agents available for continued anticoagulation.[4]

Since 2010, several DOACs utilizing newly defined and distinct mechanisms in the coagulation system have been introduced, with a better safety profile and lower bleeding risk, while providing at least equivalent efficacy to VKAs.[5,6] However, there have been several barriers to adoption of DOACs as first-line agents for oral anticoagulation, including high costs and incomplete information about clinical usage and management of complications.[7,8] Seemingly, VKAs appear to be the most common anticoagulants prescribed in clinical use, and the factors leading to physician preference in choice of initial agent are not well defined. We performed this pilot study to evaluate physician preferences in anticoagulant use and possible determinants of the same.

Methods

This study was conducted as a cross-sectional survey. The questionnaire was developed as a qualitative questionnaire to be administered through Google Forms. Initial questionnaire development was performed by a writing committee comprising of physicians from nephrology, dental sciences, and internal medicine.

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Questionnaire sequence and language were finalized discursively. Subsequently, a questionnaire review was performed by an expert board comprising three physicians from medical specialties, following which it was pretested on a group of five physicians. The questionnaire was revised and finalized based on feedback received during validation and pretesting. A total of 24 questions were finalized with the four categories as – baseline information (4 questions); clinical practice (7 questions); knowledge (9 questions); and outlook/attitude (4 questions).

The questionnaire was applied as a pilot survey among a group of five physicians to assess spelling errors and ambiguous questions, which were modified before the survey was finalized. The questionnaire was sent by E-mail and WhatsApp to intended participants, constituting physicians from various specialties and levels of experience. To ensure maximum responses, the questionnaire was distributed thrice among the intended participants. Data were compiled in Google Forms and analyzed using Microsoft Excel.

Results

Baseline data

A total of 412 physicians were contacted among various specialties (140 through E-mail and 272 through WhatsApp), of which complete responses were obtained by 50, providing an overall response rate of 12%. A majority of respondents had a subspecialty qualification including DM/MCh (*n* = 29, 58%), followed by MD/MS in 16 (32%). The site and type of practice included private medical college in 17 (34%) respondents, followed by private hospital in 16 (32%) and government medical college in 10 (20%). Most participants (*n* = 44, 88%) reported seeing more than 30 patients in outpatient clinics per week, with the majority (*n* = 33, 66%) having 2–5 patients per week on anticoagulation. Twenty-three (46%) respondents had <5 patients following up on DOACs per week while 26 (52%) had more than five. Baseline data of respondents are summarized in Table 1.

Clinical practice and perceptions

The choice of initial agent for anticoagulation was VKA in a majority of respondents (*n* = 23, 46%), followed by Dabigatran (*n* = 11, 22%). Overall, 42 (84%) participants reported ever having started DOAC for any new patient. Among those who had started a DOAC, the agent of choice was dabigatran in 24 (57%), followed by rivaroxaban in 11 (26%) and apixaban in 7 (16%). Indications for starting a DOAC included DVT/PE in 21 (50%) and atrial fibrillation in 16 (38%). While using VKAs, 44 (88%) reported requesting for a prothrombin time/international normalized ratio (INR) with each visit, but only 12 (24%) reported complete patient compliance in getting tested for INR. Table 2 summarizes salient features of queries on clinical practice.

Table 1: Baseline information on practice characteristics of respondents

Parameter	Variables	*n* (%)
Highest qualification	DM/MCh	29 (58)
	MD/MS	16 (32)
	Other post-MD fellowships	5 (10)
Type of practice	Private medical college	17 (34)
	Government medical college	10 (20)
	Private hospital >100 beds	16 (32)
	Private hospital <100 beds	3 (6)
	Private practice: Urban	3 (6)
	Private practice: Rural	1 (2)
Approximate patients in clinic per week	<30	6 (12)
	>30	44 (88)
Approximate patients on anticoagulation seen per week	2-5	33 (66)
	5 and above	17 (34)

Table 2: Characteristics of clinical practice of anticoagulants

Parameter	Variables	*n* (%)
Newly started DOACs for any patient	Yes	42 (84)
	Dabigatran	24
	Rivaroxaban	11
	Apixaban	7
	No	8 (16)
If yes, indication	Post-DVT/PE	21 (50)
	Atrial fibrillation	16 (38)
	Primary DVT prophylaxis	6 (14)
Choice of agent for young patient with unprovoked DVT	VKA	23 (46)
	Dabigatran	11 (22)
	Rivaroxaban	9 (18)
	Apixaban	3 (6)
	Not specified	4 (8)
Regular PT/INR asked at each visit on VKAs	Yes	44 (88)
	No	6 (12)
Patients missing INR tests when instructed	None	12 (24)
	Up to 1/3rd	23 (46)
	1/3rd-2/3rd	10 (20)
	>2/3rd or most patients	4 (8)

DOACs: Direct oral anticoagulants; DVT: Deep venous thrombosis; VKAs: Vitamin K antagonists; PE: Pulmonary embolism; INR: International normalized ratio; PT: Prothrombin time

On being questioned about the reason for not choosing DOACs as first-line agents, a majority (*n* = 39, 78%) indicated cost as the major barrier. Inadequate information about clinical use and management of complications was less frequent, cited by 8 (16%) respondents. Most participants (*n* = 42, 84%) said that they would continue the same DOAC without modification if a patient was referred to them for follow-up. On being asked about problems with VKAs, the most common response cited was need of regular INR monitoring (*n* = 41, 82%), followed by food-drug interactions (*n* = 7, 14%). Only 3 (6%) respondents considered bleeding to be the most important

problem with VKAs. Conversely, lack of regular blood testing was perceived to be the most attractive property of DOACs, reported by 38 (76%), followed by reduced bleeding risk by 6 (12%) and better efficacy by 5 (10%). Thirty participants (60%) indicated that even a fivefold difference in cost, if acceptable to patients, would make them prescribe DOACs as need of regular testing was obviated. Although we did not inquire about the preferred DOAC agent, most respondents (*n* = 38, 76%) indicated that twice a day administration would reduce patient compliance.

Knowledge-based questions

Most participants indicated journals as the predominant source of information on DOACs (*n* = 30, 60%), followed by conferences/meetings (*n* = 7, 14%). Pharmaceutical representatives, textbooks, and local meetings were uncommon sources and collectively constituted 12% of responses (*n* = 6). On being inquired about drugs with better efficacy, 21 (42%) selected warfarin while 26 (52%) selected DOACs. On asking about agents with a better safety profile, 43 (86%) respondents indicated DOACs to have a lesser bleeding risk than VKAs. Forty eight (96%) correctly indicated no need for regular blood testing while on DOACs. On being asked about conditions that precluded the use of DOACs, 39 (78%) correctly identified chronic kidney disease, with 5 (10%) indicating anemia and 3 (6%) ischemic heart disease as possible contraindications. Participants were also asked to respond to practice-based scenarios while using DOACs. On being asked about the best option to manage a patient in shock caused by Dabigatran-related bleeding, 15 (30%) chose fresh frozen plasma transfusion directly while 6 (12%) chose to check an activated partial thromboplastin time first. Seventeen (34%) selected looking for a specific antidote. On being asked about preoperative discontinuation of rivaroxaban, 34 (68%) correctly indicated stopping the drug 48 h preoperatively. Figure 1a illustrates responses to important perceived advantages of DOACs and Figure 1b and c to clinical scenario-based questions.

Discussion

Our study reports the results of a cross-sectional survey documenting physician preferences and determinants of the same while prescribing oral anticoagulant agents. Principal findings include a predilection toward VKAs as choice of first-line therapy, with cost being the most important barrier to DOAC usage.

Physician preference for VKAs as has been documented in several studies but is rapidly evolving as more patients receive DOACs as first-line agents.[9,10] As anticoagulation must continue for a prolonged duration, cost, safety, and tolerability become major determinants of adherence and long-term outcomes. Despite robust data on safety and efficacy of VKAs available over the past six decades,
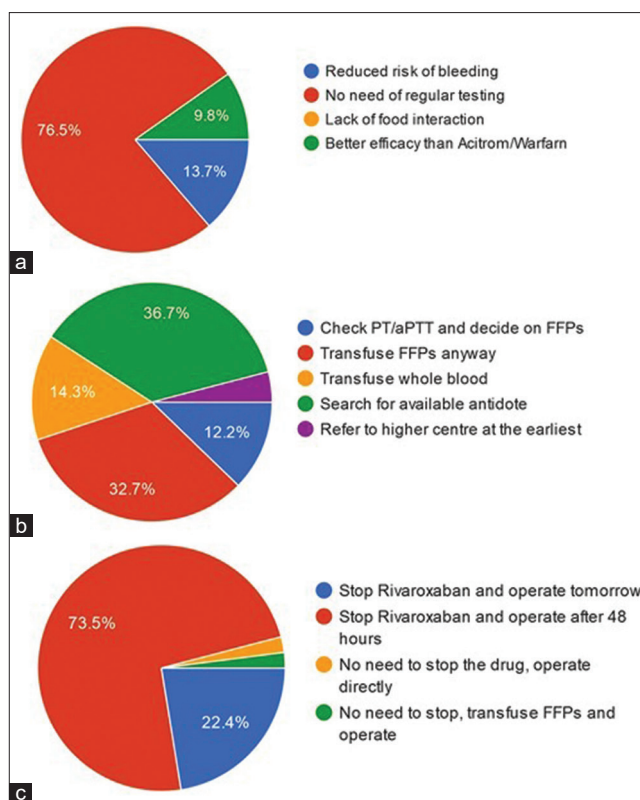

Figure 1: (a) Responses to most common perceived advantages of direct oral anticoagulants over Vitamin K antagonists, (b) Responses to the management of a critically ill patient in shock secondary to direct oral anticoagulant related bleeding, (c) Responses to preoperative management of rivaroxaban in a patient planned for elective surgery

several problems such as food-drug interactions and need for regular monitoring continue to persist. The introduction of ximelagatran in 2003 was the first step aimed to overcome these issues while maintaining equivalent efficacy compared to VKAs.[11]

A majority of respondents in our cohort identified VKAs to have better efficacy compared to DOACs, which is a predominant finding in most clinical trials comparing the two. For patients with atrial fibrillation, dabigatran,[12] rivaroxaban,[13] and apixaban[14] are found to be noninferior to VKAs for the prevention of ischemic stroke. All three agents have also been found to be noninferior to VKAs for patients for the prevention of recurrent VTE in patients receiving long-term anticoagulation.[15-17] A majority of our respondents correctly identified DOACs to have a lower risk of bleeding compared to VKAs. A lower bleeding risk is a predominant advantage of DOACs over VKAs noted in most clinical trials. In a meta-analysis including 12 studies with 77,000 patients with AF, DOACs were noted to have a 50% lower risk of major bleeding compared to VKAs.[18] A similar study including patients with VTE from six phase III trials also found a lower risk of bleeding with DOACs, while maintaining equivalent efficacy.[19]

Most participants indicated the need for regular INR monitoring to be the major disadvantage with VKAs

and can affect the time in therapeutic range with VKAs, bringing down efficacy. Strict adherence to follow-up and INR monitoring was reported to be done by less than 1/3rd patients, a finding echoed in other published data.[20] Inadequate information about clinical usage and management of adverse events with DOACs is an apparent barrier to more frequent usage. This has been reported to be equally prevalent among junior and experienced physicians.[21] Surprisingly, we did not note a significant deficit in answers to knowledge-based questions on DOACs, with most participants answering questions on preoperative use of, management of bleeding and need of testing correctly.

Cost is one of the most important factors deciding initial anticoagulant usage.[22] As of January 2021, the approximate monthly cost of warfarin at a dose of 5 mg per day is ₹ 77 (US$ 1), compared to ₹ 1500 (US$ 20) for dabigatran at 150 mg twice a day, ₹ 3900 (US$ 53) for apixaban at 5 mg twice a day, and ₹ 3810 (US$ 52) for rivaroxaban at 20 mg once a day. However, direct costs paint an incomplete picture and may be modified with the emergence of generic manufacturers. Moreover, individual agents have a variable impact on recurrent VTE, therapy-related bleeding, and quality-adjusted life years and must take cost-effectiveness into account. A meta-analysis in 2018 evaluated 11 studies comparing DOACs with VKAs and found DOACs to be uniformly more cost-effective. The incremental cost-effectiveness ratio of any DOAC agent to VKA ranged from -60000US$ to -45000 US$.[23] Among the DOACs, apixaban appears to be the most cost-effective option, with a cost avoidance of approximately US$ 4000 per patient year.[24] Indigenous cost-effective analyses including local data are essential in reaching correct inferences.

Limitations

Our study may be limited by an over-representation of specialist physicians and may not provide a true picture of barriers to DOAC usage. Although response rates of 10%–20% are typical for a complex survey, a response rate of 12% noted by us may not provide a representative picture.[25]

Conclusions

Our survey illustrates physician preferences in choosing initial oral anticoagulants and indicates lack of INR monitoring and better safety as the predominant advantages perceived with DOACs. Within our cohort of specialist physicians, knowledge about DOACs does not appear to be a major limiting factor and cost emerges as the predominant barrier for more frequent use.

Ethical clearance

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Conflicts of interest

There are no conflicts of interest.

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