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Haematology International Journal
ISSN: 2578-501X

A Survey of Clinicians Practice Patterns in Anticoagulation Therapy & Prophylaxis in Nigeria

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Research Article
Volume 2 Issue 1
Received Date: June 14, 2018
Published Date: June 29, 2018
DOI: 10.23880/hij-16000125

Abstract

Introduction: Therapeutic and prophylactic anticoagulation is under-prescribed in Nigeria, Dismal practice patterns of anticoagulation, lack of hospital-based anticoagulation policy may be contributory

Objective: The aim was to evaluate clinicians practice patterns in anticoagulation therapy and prophylaxis in Nigeria.

Materials and Methods: The study was a multi-centre survey using pretested validated questionnaire administered to 528 clinicians in some tertiary hospitals in South East Nigeria. The primary outcome measure was the practice pattern of anticoagulation therapy and prophylaxis. A p-value < 0.05 was considered as statistically significant. Data analysis was with Statistical Package for Social Science (SPSS) software, version 18 (SPSS Inc., Chicago, IL)

Results: We discovered that only 52 respondents (9.8%) claimed their institutions had an anticoagulation policy. The most prescribed anticoagulation agent was low molecular weight heparin (LMWH), (AOR 163, 95% CI 0.85-0.3.14, P=0.19) while the fondaparinux was least prescribed (AOR 1.74, 95% CI 0.61-5.0 P=0.44). Only 193 (36.6%) of the respondents routinely prescribed anticoagulation therapy when indicated. Those with 15-20 years clinical experience identified cost is an important determinant in prescribing anticoagulation agents. (P=0.06, 95%CI 0.94 -12.4)

Conclusion: The study showed the need to establish policy or guideline driven dedicated anticoagulation clinic services as well as practice-oriented CMEs to stem anticoagulation-related morbidity and mortality.

Keywords: Anticoagulation Therapy; Prophylaxis; Fondaparinux

Abbreviations: DOAC: Direct Acting Oral Anticoagulants; DVT: Deep-Vein Thrombosis; ICH: Intracranial Haemorrhage; PE: Pulmonary Embolism; SPSS: Statistical Package for Social Science; DAC: Dedicated Anticoagulation Clinics; AF: Atrial Fibrillation; OAC: Oral Anticoagulation; LMWH: Low Molecular Weight Heparin.

Introduction

Anticoagulants prevent the formation of thrombi that can form in the veins, arteries or intracardial with its attendant complications through obstruction, embolisation and consumption of haemostatic proteins [1]. The target-specific direct acting oral anticoagulants (DOAC) are more efficient and safer compared to older and widely used vitamin k antagonists (for example, warfarin) in the prevention of stroke and systemic embolism in patients with atrial fibrillation, and for the treatment of venous thromboembolism [2]. They do not require routine monitoring; they also do not have food or drug interactions [3]. The significant drawbacks of the DOACs include their high cost and lack of a specific antidote [3]. Though recently FDA has announced new reversal agents for dabigatran and rivaroxaban [4,5]. In the absence of anticoagulation therapy, the risk of deep-vein thrombosis (DVT) in medically ill patients is comparable to that in moderate-risk surgical patients [6]. The decision to commence anticoagulation therapy usually involves the use of bleeding risk predictable outcome tools like HAS-BLED [7] (Hypertension, Abnormal renal function, abnormal liver function, Stroke Bleeding Labile INR, Elderly, Drugs) and CHA2D2S2-VASc (Congestive cardiac failure, Hypertension, Age2 Diabetes, Stroke, Vascular disease, Sex female [8]. These guidelines ensure that patients who would benefit from anticoagulation, get them and excludes patients who will not find anticoagulants useful while keeping the incidence of complications like bleeding to the lowest tolerable level. Hence the decision to implement anticoagulant therapy in atrial fibrillation to improve outcome requires balancing the decreased risk of stroke against the increased risk for intracranial haemorrhage (ICH) [9].

Clagett, et al. showed that thrombo-prophylaxis reduced the risk of DVT and pulmonary embolism (PE) [10]. There are also guidelines for the management of thromboembolic phenomenon which have been in place for many years, but anticoagulants remain underused throughout the world [11-13]. Centre for Outcomes Research at the University of Massachusetts Medical School (UMMS) conducted ENDORSE (Epidemiologic International Day for the Evaluation of Patients at Risk for Venous Thrombo-embolism in the Acute Hospital Care Setting) study. A cross-sectional survey of VTE risk and prophylaxis provision in the acute care hospital setting using data provided by 358 hospitals in 32 countries [14]. It showed a significant percentage of patients were at risk of DVT, but only 58.5% of at-risk surgical and 39.5% of at-risk medical patients received appropriate thrombo-prophylaxis [14]. Many other studies have supported these findings [15,16]. It is surprising that anticoagulants are still underutilised to this degree.

Previous studies have revealed grossly inadequate knowledge and a dismal practice of anticoagulation among healthcare workers [7,8,17,18]. The story is, however, different in North America were over 2 million people were either receiving or had benefited from anticoagulation as at 2012 [19]. Prophylactic anticoagulation is under-prescribed in South Africa, as well as in many countries in Africa [6]. Kesieme, et al. reported that 33.3% of surgeons had good knowledge of anticoagulation prophylaxis, while only 20% had a good practice of anticoagulation among the surgeons in tertiary hospitals in Nigeria [19].

The study aimed to evaluate the practice of anticoagulant therapy; determine anticoagulants agents used, the criteria for their prescription including which group of patients that will benefit from thrombo-prophylaxis. The study also documented the frequency of drug-induced complications resulting from the use of anticoagulants and if there is an anticoagulation policy in the hospitals surveyed.

Methodology

The present study was a multi-centre cross-sectional survey of the practice of anticoagulant therapy among clinicians in South East Nigeria from September 2016-February 2017. Trained research assistants distributed

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six hundred pretested multiple-choice self-administered questionnaires administered to clinicians (consultants specialist senior registrars, registrars and house-officers) in six tertiary hospitals in South East Nigeria. The questionnaire was to assess their practices in anticoagulation therapy. A pilot study checked for clarity and consistency of questions. The questionnaires were administered consecutively to clinicians in the participating centres. The following institutions participated in the survey: University of Nigeria Teaching Hospital Enugu, Federal Medical Centre Umuahia, Federal Teaching Hospital, Abakaliki, Abia State Teaching Hospital Aba, Nnamdi Azikiwe Teaching Hospital Nnewi, Federal Medical Centre Owerri and Chukwuemeka Odumegwu Ojukwu Teaching hospital, Amaku Awka. It was a two-part questionnaire and respondents were required to fill in their age, gender, number of years since graduating, speciality or grade and other parts consisted of questions on the practice of anticoagulation in their centres. We distributed anonymised questionnaires (omitting names of respondents and participating health institution) during clinical meetings, seminars, grand-rounds. Institution research ethics committee approved this study. We included tertiary healthcare institutions with residency training programme and excluded non-tertiary healthcare institutions without residency programme. Descriptive statistics with counts and percentages were used to illustrate the results. The data were also analysed using student t-test, and Fisher's exact test was used to detect any association between demographic profiles and anticoagulation practices patterns among respondents. A logistics analysis was used to detect any association between demographic background, practice patterns and anticoagulation management. A p-value< 0.05 was statistically significant. Data analysis was with Statistical Package for Social Science (SPSS) software, version18 (SPSS Inc., Chicago, IL).

Results

Practice Settings

Of the six hundred questionnaires distributed, a total of 528 clinicians completed the questionnaires (88% response rate). There were more males 378/528 (71.6%) than females, 150/528(28.4%) among the respondents. We showed that the clinicians who practised for fewer than5years are in the majority 189/528 (35.8%) and those with 15-20years of practice 46/528 (8.7%) are in the minority. The junior residents formed major part 164/528 (31.1%), and the consultants are the least of the respondents 109/528 (20.6%) (Table 1).

Years of practice of respondents	Number (%)
<5	189(35.8)
6-10	159(30.1)
11-15	85(16.1)
16-20	46(8.7)
>20	109(20.6
Grade of clinicians	
House officers	118(22.3)
Junior residents	164(31.1)
Senior residents	137(25.9)
Consultants	109(20.6)

Table 1: Some demographic characteristics of the respondents.

Institution-Based Anticoagulant Policy and Use of Guidelines

Only 498 out of 528 clinicians (94.3%) responded to this query. The result showed that only 52 of 498 respondents (10.5%) claimed their institutions had some form of anticoagulation policy and used guidelines in their practice. Only 274/494 (55.5%) of them said they did not use guidelines and they had no such institutional anticoagulation policy, and 168 (34.0%) responded "do not know" to that question.

Does your hospital have an anticoagulation policy?	Number of respondents (percentage)
Yes	52(9.8%)
No	274(51.9%)
Do not know	168(31.2%)
Anticoagulation agents (AA) prescribed	
Unfractionated heparin	511 (96.8%)
Warfarin	502(95.1%)
Low molecular weight heparin	406(76.9%)
NOAC	235(44.5%)
Fondaparinux	222(42%)
Complication	
Bleeding	492(93.2%)
Heparin-induced thrombocytopenia	109(20.6%)
Osteoporosis	5(0.9%)
Skin necrosis	4(0.8%)
Jaw necrosis	1(0.2%)
Derangements of liver enzymes	Nil
Any other complication	Nil

Table 2: Clinicians response to some questions on practice of anticoagulation.

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Table When there are no definite policies the practice of anticoagulation therapy and or prophylaxis are likely to be less than ideal with resultant increase in patient morbidity and mortality (Table 2).

Clinicians Prescription Pattern Factors Affecting

Clinicians used and prescribed low molecular weight heparin most frequently (OR=1.63, 95%CI=0.85-3.14, P=0.44) and fond aparinux was the most infrequently used (OR=1.74 95%CI=0.61-5.0 P=<0.0001) (Table 3). The consultants prescribed heparin and warfarin most, with the newer anticoagulants taking the rear position. Only 193/521(37.0%) of the respondents routinely prescribed anticoagulation therapy when indicated. Multinomial logistic regression showed that clinicians with <5 years of clinical practice; "don't feel it is important to prescribe anticoagulation therapy or prophylaxis when indicated" (P, 0.005 95% CI, 1.3-3.7). Respondents with 15-20 years clinical practice identified cost is an essential variable in prescribing anticoagulation agent (P, 0.062 95% CI, 0.94-12.4) (Tables 4-6).

Clinicians who prescribed AA when indicated	Anticoagulants	AOR	P value	95% CI	
				Lower bound	Higher bound
Consultants	UF	2.79	0.0006	1.57	4.94
	Warfarin	0.5	0.02	0.28	0.88
Non Consultants	LMWH	1.63	0.19	0.85	3.14
	Fond aparinux	1.74	0.44	0.6	5
	NOACS	0.94	1	0.46	1.9

Table 3: Prescription pattern of anticoagulants among clinicians.

Factors that affect prescription pattern	Likelihood Ratio Tests		
	Chi-Square	df	P valve
Do not feel it is important to prescribe	14.738	4	.005
Risk of prescription outweighs the benefit	17.374	4	.002
The cost is prohibitive	12.564	4	.014
It is not a policy of our hospital	4.694	4	.32
My seniors gives contrary instruction on prescription	8.067	4	.089

Table 4: Factors that affects Clinicians prescription pattern of anticoagulation agents.

Years of practice	Factors that affects prescription pattern	P value	Exp(B)	95% Confidence Interval for Exp(B)	
				Lower Bound	Upper Bound
<5	Don't feel it is important to prescribe	**.003**	**2.203**	**1.300**	**3.731**
	Risk of prescription outweighs the benefit	.262	.632	.283	1.409
	The cost is prohibitive	.457	.549	.489	4.905
	It is not a policy of our hospital	.358	.593	.195	1.806
	My seniors' gives contrary instruction on prescription	.822	.871	.263	2.891
05-Oct	Don't feel it is important to prescribe	**.026**	**1.832**	**1.074**	**3.123**
	Risk of prescription outweighs the benefit	.577	1.25	.57	2.741
	The cost is prohibitive	.423	1.615	.501	5.211
	It is not a policy of our hospital	.799	.864	.281	2.655
	My seniors' gives contrary instruction on prescription	**.052**	.215	**.045**	**1.017**
Oct-15	Don't feel it is important to prescribe	.673	1.132	.635	2.018
	Risk of prescription outweighs the benefit	.523	.748	.307	1.823
	The cost is prohibitive	**.014**	**4.292**	**1.338**	**13.762**
	It is not a policy of our hospital	.789	1.174	.364	3.792

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	My seniors' gives contrary instruction on prescription	**.076**	.199	.033	1.187
15-20	Don't feel it is important to prescribe	.145	1.642	.843	3.2
	Risk of prescription outweighs the benefit	.129	.404	.126	1.302
	The cost is prohibitive	**.062**	**3.415**	**.939**	**12.415**
	It is not a policy of our hospital	.985	.987	.257	3.79
	My seniors' gives contrary instruction on prescription	.174	.209	.022	1.997

Table 5: Multinominal logistics analysis of factors that affects prescription patters based on years of practice.

Reason	Number of respondents(percentage)
Do not feel it is important to prescribe	484(91.7%)
Risk of prescription outweighs the benefit	412(78%)
The cost is prohibitive	439(83.1%)
It is not a policy of our hospital	469(88.8%)
My seniors give contrary instruction on prescription	492(93.2%)

Table 6: Showing reasons why clinicians do not prescribe anticoagulation prophylaxis routinely as required.

Anticoagulation Management

Anti-coagulation treatment and prophylaxis were the most frequently used for patients with prolonged surgery 168/520 (32.3%). Sixty-three percent of respondents 63/520 (12.5%) were unsatisfied while 219/504 (43.4%) were not very satisfied with the laboratory monitoring tools available in their institutions. Bleeding was the most common complication of anticoagulation among the respondents 383/492(77.9%). The least encountered complication was jaw necrosis 57/479 (11.9%).

Discussion

The non-existent anticoagulation policy in our various healthcare institutions and disuse of anticoagulation management practice guidelines in Nigeria is probably responsible for the less than ideal standard care received by Nigerians needing anticoagulation. The few anticoagulation services available appear not to be protocol or guideline-driven, unorganised, poorly funded, and inadequately equipped. Anticoagulation policies help define and guide the establishment and success of dedicated anticoagulation clinics (DAC). Lack of hospital-based anticoagulation policies have led to no dedicated anticoagulation services or where offered, are substandard and not according to best practices. In Nigeria, observational evidence and experiences from most clinicians in tertiary healthcare institutions are that absence of dedicated anticoagulation clinics in their centres. However, some sub-Saharan African countries now have DAC notably Kenya and South Africa [20,21]. A well-articulated anticoagulation policy could have pharmacists, nurses and family physicians manage DAC under the supervision of haematologists and or cardiologists.

In our survey, we also found that there was a low number of the respondents who routinely prescribed anticoagulation therapy when indicated in this study. A probable reason for this unsafe practice may be the fear of bleeding, which is the most frequent complication of anticoagulation therapy inform the hospitals included in this survey. No doubt, bleeding from over anticoagulation is a real danger, but it is worse where there is no dedicated anticoagulation clinic and suboptimal blood transfusion support. The low prescription rate in this survey was also in keeping with the belief of the respondents that the risk of anticoagulation outweighs the benefits and strengthened by the acceptance that the cost was an important variable in prescribing anticoagulation agents. It may not come as a surprise that few respondents were favourably disposed to prescribing anticoagulants given that majority of them reported that their institutions had no anticoagulation policy.

Unfractionated heparin was the most frequently, and fond aparinux was the most infrequently prescribed for therapeutic and prophylactic indications among the clinicians. The plausible reason may be that NOACsis still relatively unknown in our environment and not readily available and accessible. NOAC is also more expensive than conventional anticoagulants. Continuous medical education, together with viable insurance schemes that will discourage out of pocket spending by patients may improve the prescription of NOACs for anticoagulation treatment and prophylaxis.

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Understandably, prolonged surgery, the risk of DVT and immobilisation form the highest indications for the prescription of anticoagulants in the centres surveyed. Atrial fibrillation (AF), rheumatic heart disease and mechanical valves and atrial fibrillation (AF) were the least indications for anticoagulation among clinicians in this study. AF remains one of the major causes of stroke, heart failure, sudden death, and cardiovascular morbidity in the world [22]. Current guidelines state that oral anticoagulation (OAC) is a cornerstone therapy in the management of AF. Surprisingly, heart failure was not on the list of indications for the prescription of anticoagulants despite its high prevalence in the sub-Saharan African countries [23]. Heart failure and AF coincide in many patients [24-26]. They are also linked to similar risk factors and share a common pathophysiology [27]. Heart failure with reduced ejection fraction has increased the risk of thromboembolic events. The use of OAC in heart failure with AF is not debatable, but their use in heart failure in sinus rhythm has been contentious [28]. The current consensus is that there is no convincing data to support the use of anticoagulation with VKAs because of the increased rate of bleeding among these patients even though that VKAs significantly reduced the rate of ischaemic strokes [29-32].

Anticoagulation has been shown to be important, appropriate and capable of reducing complications among the rheumatic heart disease populations. Fleming, et al. showed a marked reduction of VTE incidents in patients with rheumatic heart disease compared to untreated patients with RHD [31]. Although the clear benefits of VKA therapy in patients with RHD, very few patients have access to systematic anticoagulation management in resource-constrained settings where RHD is most prevalent [33,34].

No respondent mentioned HIV as an indication for anticoagulation in this survey. Currently millions of patients throughout sub-Saharan Africa are now receiving care for HIV [22]. Previous investigations have revealed an almost four-fold increase in the risk for DVT among HIV-infected populations compared to general populations [22]. As HIV care programs continue to grow and expand throughout sub-Saharan Africa, there must also be a focus on developing the infrastructure for many of the complementary aspects of HIV care, such as anticoagulation monitoring to ensure patients have access to all essential aspects of care [35].

Bleeding is a significant adverse effect of anticoagulation. Our survey showed the trepidation which is associated with bleeding as almost all respondents chose this option as the main drawback to anticoagulation. A significant concern expected when there is no anticoagulation policy and no dedicated anticoagulation clinic available. In fact, centres with DAC have low complications and manage such complications. A South African study, showed a low incidence of bleeding complications in a study population, some of the bleeding episodes resulted from drug-drug interactions [23]. The prevalence of significant bleeding associated with the use of LMWH for prophylaxis and VTE treatment is low compared to other anticoagulant agents like UFH, fond aparinux [36-39].These data suggest a manageable incidence of bleeding in centres with DAC. The concern for bleeding should not deny patients in need of anticoagulation, the benefits of life-saving effects of anticoagulants.

Globally, management of anticoagulation therapy presents a significant problem for clinical and laboratory services [38], only a DAC can match such challenges. The issue of cost also impacts negatively on the practice of anticoagulation. In the background of poor socioeconomic factors and infantile medical insurance scheme, with many uninsured, out of pocket expense continuously hinders patients' compliance and adherence to the use of anticoagulants especially the NOACs [39].

Conclusion

This survey has shown the lack of anticoagulation policies and use of anticoagulation guidelines among the centres that participated. The practice of anticoagulation must follow international guidelines and best practices to be beneficial to patients. Our survey has also shown deficiencies in practice patterns of the clinicians for anticoagulation therapy in South East Nigeria. These gaps can be remedied by continuous medical education, by the establishment of anticoagulation policies and guideline-driven dedicated anticoagulation clinics (DAC).

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