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Assessment of adherence level of patients on anticoagulant therapy in a tertiary healthcare facility in Uyo, Nigeria

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Abstract

Background: Anticoagulants are highly effective in preventing venous thromboembolism and remains the main stay of treatment. However, strict adherence to medication is essential for maximizing treatment.
Objectives: the objectives of this study, were to determine the adherence rate and factors that may influence adherence to anticoagulant therapy among patients on anticoagulant at a tertiary healthcare facility in Uyo, Nigeria.
Methodology: This was a cross-sectional study. Fifty-nine consented adult patients on anticoagulant therapy were recruited consecutively into the study. A structured self-administered questionnaire was used to obtain information on respondents sociodemographic characteristics, indications for anticoagulation and types of anticoagulant used. An 8-item Morisky Medication Adherence Scale (MMAS-8) was used to assess patient's adherence to anticoagulation therapy.
Results: The mean age of respondents was 55.4±13.5 years. Thirty-three (55.9%) were males while 26 (44.1%) were females. The most common indication for anticoagulant use was for treatment of deep vein thrombosis (78%). The direct oral anticoagulant (DOAC) was the most frequently used anticoagulant (76.3%), and majority (44.1%) had treatment for 3 months. Overall, 49.1% of the respondents had unacceptably low level of adherence while 10% had high level adherence to anticoagulant use. The female gender and the duration of anticoagulant were significantly associated with the level of adherence.
Conclusion: Adherence to anticoagulant use among respondents in this study was suboptimal. The female gender and the duration of anticoagulant were significantly associated with the level of adherence.

Keywords: Adherence, Anticoagulant, Venous thromboembolism.

Introduction

Venous thromboembolism (VTE) is major cause of morbidity and mortality globally.[1] An incidence of between 60,000 to 100,000 have been reported to occur annually by Centre for Disease Control (CDC) in United State with about 5-8% of the population having one genetic risk factor.[2] A post mortem review in Nigeria put the VTE prevalence at about 3% or less.[3]

Although, global audit reveals sub-optimal use of thromboprophylaxis even in high risk patients[4,5] nonetheless, the number of patients on anticoagulant therapy have increased remarkably in the last decade due to its proven efficacy and improved safety profile[6] However, the optimal length or duration of therapy remains somewhat uncertain. However, a general consensus and recommendation has been to treat patients with oral anticoagulant (OAC) for at least 3-month following an episode of DVT/PE except where there are obvious contraindications.[7] Furthermore, decision to stop anticoagulant at 3-months or to treat

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indefinitely depends on several factors including; risk of recurrence, risk of bleeding and patient preferences.[7]

Despite the fact that anticoagulants are highly effective in preventing VTE and remains the main stay of treatment, strict adherence to medication is essential for maximizing treatment benefits. World Health Organization (WHO) defines adherence as "the extent to which a person's behaviour-taking medication, following a diet and/or executing a lifestyle changes, corresponds with agreed recommendations from a healthcare provider".[8] This definition emphasises that the patients is equally an active collaborator in his/her treatment.

Various studies have been done to determine the level of adherence of patients on oral anticoagulants to therapy.[9-11] In a survey by Patel et al.,[9] to determine the OAC adherence rate of patients on direct oral anticoagulants (DOAC) and warfarin for treatment of atrial fibrillation (AF) and VTE, the authors found no significant difference in the adherence rate between the two groups. Also, the results from a systemic review and meta-analysis of adherence to OAC therapy among patients with atrial fibrillation showed that up to 30% of patients were not adherent to therapy.[10] Furthermore, Yao et al,[11] in their study reported that adherence to OAC therapy was poor, but that modest improvement could be achieved with the use of DOAC. This is because these agents (DOAC), have the following advantages among others; easy dosing, fewer drug-drug interactions, and little or no monitoring.[11]

Several reasons have been adduced to why patients do not often adhere to their medications. These include but not limited to the following; socio-economic factors (poor economic status, high cost of medication); patient factors (forgetfulness, treatment anxiety, lack of understanding of medication instruction); drug related factors (adverse effect of the drug, duration of drug treatment), disease related factors (nature of disability, severity of the disease).[12]

The observed increase in the number of patients with recurrent thromboembolic diseases in our centre many of whom are on anticoagulant therapy have necessitated this study couple with the paucity of literature on adherence to anticoagulant medications in our environment.

Therefore, the objectives of this study were to determine the adherence rate and factors that may influence adherence to anticoagulant therapy among patients on anticoagulant at a tertiary healthcare facility in Uyo, Nigeria.

Materials and methods

Study Site

This study was conducted in the Department of Haematology, University of Uyo Teaching hospital, a tertiary referral hospital in the South-South region of Nigeria. The Department runs a general haematology clinic where patients with various haematological disorders including those with venous-thromboembolic diseases are managed. It also collaborate with other departments in the hospital in the management of patient on anticoagulants.

Study Design/ Study Population

This was a descriptive cross-sectional study to determine the set objectives of the study. Respondents were patients attending haematology clinic and were on oral anticoagulant therapy for at least one month for the management of VTE.

Inclusion/Exclusion Criteria

All Respondents aged 18- years and above with complete clinical records, who were on any of the anticoagulant medications for at least 3 months and who signed an informed consent were recruited into the study. Respondents less than 18 years of age, with incomplete clinical records and who did not give consent were excluded from the study.

Data Collection

Data was collected using a structured and self-administered questionnaire. The questionnaire was administered to the subjects during clinic visits and collected as soon as it was completed. Measures evaluated include; socio-demographic characteristics of subjects, indications for anticoagulation therapy, types of anticoagulant medication and duration of anticoagulant therapy. An 8-item Morisky Medication Adherence Scale (MMAS-8) was used to assess patient's adherence to anticoagulation medication.[13]

Data Analysis

Data was analysed using SPSS for windows version 20 and presented in simple tables. Descriptive

statistics was done for continuous variables while categorical variables were compared using chi-square. Level of significance was set at 5% ($p< 0.05$).

Results

The mean age of respondents was 55.4±13.5 years. Thirty three (55.9%) were male while 26 (44.1%) were females. More than half 32(54.2%) were above 55 years. A good proportion 23 (39%) were civil servants, more than half (57.6%) had tertiary level of education.

The most common indication for anticoagulant use was for treatment of DVT (78%). The direct oral anticoagulant (DOAC) was the most frequently used anticoagulant (76.3%), followed closely by low molecular weight heparin (LMWH) (35.6%) an injectable anticoagulant. For majority (44.1%) of respondents, duration of treatment was 3-months while less than 20% had treatment extending beyond one year duration. (Table 2).

Using the 8-items Morisky medication adherence scale, 49.1% of the respondents had unacceptably low level of adherence while just 10% had high level of adherence to anticoagulant use. Table 3.

Majority of the respondents (81.4%) attributed their non-adherence to the high cost of the drugs. This was followed by busy work schedule (32.2%) and fear of possible bleeding complication (30.5%). Only 35.6% of the respondents alluded to taking their medication regularly. Table 4

From univariate analysis, female gender and the duration of anticoagulant use were the two variables that showed significant association with the level of adherence. ($p=0.01$ and 0.03 respectively). Table 5

Table 1: Socio-demographic characteristics of Respondents

Variables	Frequency	Percent
Age (in years)		
Less than 55	27	45.8
55 and above	32	54.2
Mean+/- standard deviation	55.4+/-13.5	
Sex		
Male	33	55.9
Female	26	44.1
Education		
Primary	9	15.3
Secondary	16	27.1
Tertiary	34	57.6
Occupation		
Self employed	19	32.2
Civil servant	23	39.0
Student	1	1.7
Retired	16	27.1
Marital status		
Single	2	3.4
Married	55	93.2
Divorced	2	3.4

Table 2: Indications for and type of Anti-Coagulant Use among respondents

Variables	Frequency	Percent
Deep vein thrombosis (DVT)	46	78
Pulmonary embolism (PE)	3	5.1
DVT/PE	10	16.9
Duration of anticoagulant therapy (in months)		
1-3	26	44.1
4-6	14	23.7
7-12	17	28.8
Above 12	2	3.4
***Type of anticoagulant used**		
Direct oral anticoagulant (DOAC)	47	78.0
Low Molecular Weight Heparin (LMWH)	21	35.6
Warfarin	10	16.9

*Multiple responses allowed

Discussion

Oral anticoagulants are highly effective for the prevention of venous thromboembolic events. However, strict adherence to medication is very important for maximizing treatment benefit. Majority of the respondents in this study had suboptimal adherence level to oral anticoagulant therapy. Using the 8-item MMAS, almost half (49.1%) of the respondents had low adherence, 40.7% had medium adherence and just 10% took the medication consistently. Our findings contrast the studies by Davis et al.[14] and Avila et al.,[15] in the former study, more than half of the respondents were reported to have adequate adherence level while in the later study, more than 40% of the respondents had high level of adherence with only 3% having low adherence level. But, unlike this present study, both studies made use of the 4-item MMAS to measure adherence level. Studies have shown that scores of both MMAS (4-item and 8-item) show similar quantitative and qualitative characteristics, suggesting that data sources from both scales could be integrated.[16] On the other hand, the low adherence to anticoagulant therapy among our respondents was consistent with the findings of other authors.[11,17] Anticoagulants are often initiated as preventive measures largely to prevent further thrombus formation or the re-occurrence of new thrombus without necessarily addressing any remote symptoms. Hence, the likelihood of nonadherence could be relatively high since their symptoms may not be addressed by taking them.

Several studies have identified various factors responsible for nonadherence to anticoagulant therapy.[12,18-19] These have been reported to include; forgetfulness, other priorities, personal decision to skip doses, misunderstanding of the dosing regimen, and emotional factors among others. Many of these factors are patients' related behaviour and are similar to that reported in this study. In decreasing order of occurrence, high cost of drugs, forgetfulness from busy work schedule and fear of bleeding from prolonged use of oral anticoagulant were the commonest reasons for nonadherence to anticoagulant therapy in this study. High cost of medication is undoubtedly a major mitigating factor to adherence especially in developing clime like ours where access to drug is still very much limited.[20] Also, forgetfulness arising from a busy work schedule may very well reflect various

Table 3: 8-Item Morisky Medication Adherence Scale Assessment and Respondents Level of Adherence

Variables	Frequency	Percent
Do you sometimes forget to take drugs?		
Yes	33	55.9
No	26	44.1
Did not take my medications on any days within the past 2 weeks?		
Yes	26	44.1
No	33	55.9
Ever stopped taking your drugs without telling your doctor because you felt worse?		
Yes	11	18.6
No	48	81.4
When I travel or leave home, I sometimes forget to bring my drugs along?		
Yes	21	35.6
No	38	64.4
Did you take your drug yesterday?		
Yes	17	28.8
No	42	71.2
When you feel sometimes that your symptoms are under control, do you sometimes stop taking your drugs?		
Yes	14	23.7
No	45	76.3
I feel hassled about sticking to my drugs religiously		
Yes	35	59.3
No	24	40.7
How often do you have difficulty remembering to take all your medication?		
Once in a while	31	53.5
Never/rarely	27	46.5
sometimes	-	-
Adherence levels		
High	6	10.2
Medium	24	40.7

Table 4: Reasons for respondents not taking their drugs regularly

Reasons	Frequency	Percent
None, I take my drugs regularly		
Yes	21	35.6
No	38	64.4
High cost of drugs		
Yes	48	81.4
No	11	18.6
My very busy schedule makes me forget		
Yes	19	32.2
No	40	67.8
Fear of bleeding complication from prolong drug use		
Yes	18	30.5
No	41	69.5
Too frequent monitoring of the drug thus adding to the cost		
Yes	9	15.3
No	50	84.7
Too many drug restrictions as a result of drug use		
Yes	5	8.5
No	54	91.5
Taking the drug for a very long time		
Yes	11	18.6
No	48	81.4

competing interest which takes precedence over adherence to medication. Furthermore, the perceived fear of bleeding also contributed nonadherence to anticoagulant therapy by some of the respondents in this study. The perceived risk of bleeding have been reported to not only affect the odds of oral anticoagulant use, but were also associated with the timing of oral anticoagulant initiation and the likelihood of discontinuation.[21] Using the ''HAS-BLED Score'' a therapeutic bleeding risk stratification score for those on oral anticoagulant in atrial fibrillation, shows that a score $\geqslant 4$ is associated with a higher likelihood of a patients on oral anticoagulant to default on therapy.[21] However, there was no statistically significant differences between these variables (high cost of medication, forgetfulness from busy schedule and fear of bleeding) and the level of adherence; perhaps the small sample size of respondents in this study may have accounted for this observation.

Comparatively the female respondents had a relatively better adherence level compared to their male counterparts and this was statistically significant (p=0.01). Our findings agree with that of

Table 5: Association between selected socio-demographic/clinical characteristics and level of adherence among respondents

Variables	Levels of Adherence			Total n (%)	P Values
	High	Medium	Low		
Sex					Fisher's exact =0.01*
Males	0 (0.0)	16 (66.7)	17 (58.6)	33 (55.9)	
Females	6 (100.0)	8 (33.3)	12 (41.4)	26 (44.1)	
Age group (in years)					Fisher's exact =0.12
Less than 55	1 (16.7)	9 (37.5)	17 (58.6)	27 (45.8)	
55 and above	5 (83.3)	15 (62.5)	12 (41.4)	32 (54.2)	
Education level					Fisher's exact =0.24
Primary	2 (33.3)	5 (20.8)	2 (6.9)	9 (15.3)	
Secondary	1 (16.7)	8 (33.3)	7 (24.1)	16 (27.1)	
Tertiary	3 (50.0)	11 (45.8)	20 (69.0)	34 (57.6)	
Occupation					Fisher's exact =0.44
Self employed	1 (16.7)	10 (41.7)	8 (27.6)	19 (32.2)	
Civil servants	3 (50.0)	6 (25.0)	14 (48.3)	23 (39.0)	
Students	0 (0.0)	0 (0.0)	1 (3.5)	1 (1.7)	
Retired	2 (33.3)	8 (33.3)	6 (20.7)	16 (27.1)	
Duration (in months)					Fisher's exact =0.03*
1-3	4 (66.7)	15 (62.5)	7 (24.1)	26 (44.1)	
4-6	2 (33.3)	3 (12.5)	9 (31.0)	14 (23.7)	
7-12	0 (0.0)	6 (25.0)	11 (37.9)	17 (28.8)	
Above 12	0(0.0)	0 (0.0)	2 (6.9)	2 (3.4)	
High cost					Fisher's exact =0.22
Yes	5 (83.3)	17 (70.8)	26 (89.7)	48 (81.4))	
No	1 (16.7)	7 (29.2)	3 (10.3)	11 (18.6)	
Busy job schedule					Fisher's exact =0.12
Yes	1 (16.7)	5 (20.8)	13 (44.8)	19 (32.2)	
No	5 (83.3)	19 (79.2)	16 (55.2)	40 (67.8	
Fear of complication					Fisher's exact =0.10
Yes	0(0.0)	6 (25.0)	12 (41.4)	18 (30.5)	
No	6 (100.0)	18 (75.0)	17 (58.6)	41 (69.5)	

Castellucci et al.[22] who in their study on the assessment of self-reported anticoagulation adherence using the 4-items Morisky scale, found that the female genders amongst other variables was a predictor of anticoagulation adherence and was significantly associated with better anticoagulation adherence. However, our finding contrasts the findings by other authors. Hernandez et al.,[21] in their study identified sex as an important predictor of oral anticoagulant adherence amongst other demographic variables. However, the female gender in this case was associated with a higher odd of nonadherence to their oral anticoagulant. Borne RT et al.,[23] also identified sex as an important predictor of oral anticoagulant adherence with the female gender having a lower or reduced odd of oral anticoagulant adherence compared with their male counterpart.[23]

The nonadherence to medication is more apparent in long-term chronic diseases where treatment is often geared toward prevention and may provide little or no symptomatic relief for the patient. There was a statistically significant association between the duration of OAC use and the level of adherence of the respondents in this study (p=0.03). Osterberg L et al.[24] observed that adherence is higher during treatment of an acute condition, but decrease significantly after the first 3 month of treatment for chronic or long-term condition. Also, findings from some randomise clinical trials (RTCs) have shown that some patients struggle to maintain anticoagulation with the DOAC over long-term and that a good proportion of them discontinue therapy even before the end of treatment.[25,26] A major reason for this is that DOAC do not require routine monitoring of anticoagulant activity. However, a more probable reason that could be adduce to nonadherence to prolonged anticoagulant use from this study is the high cost of medication. Healthcare financing is predominantly out-of- pocket payment in our environment.[27] Majority of our respondents are in the low-income bracket with fixed income. Hence, ability to sustained treatment over a long period is limited. Hence, they may choose to discontinue therapy even before the end of treatment. An important limitation of this study is it small sample size and its cross-sectional nature which does not allow for the evaluation of anticoagulant adherence change overtime.

Conclusion

Adherence to anticoagulant therapy among respondents in this study was suboptimal as close to 50% had poor adherence. The female gender and the duration of anticoagulant were significantly associated with the level of adherence.

Conflict of Interest: The authors declare no conflict of interest.

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