ORIGINAL RESEARCH

ASSESSMENT OF KNOWLEDGE OF ANTICOAGULATION THERAPY (WARFARIN) AND INR CONTROL AMONG OUTPATIENTS IN A TERTIARY HOSPITAL IN LAGOS, NIGERIA

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ABSTRACT

Background: There is a general consensus in the literature that improved patient knowledge about warfarin therapy improves therapeutic outcomes.[1] Some studies have associated inadequate knowledge of warfarin use by patients to poor anticoagulation control, increased recurrence of haemorrhagic events and non-adherence[2] however, no known published article exists on knowledge base of warfarin users in Nigeria. The objective of this study was to assess the knowledge level of patients receiving warfarin therapy for anticoagulation in an outpatient cardiology clinic using validated Anticoagulation Knowledge Assessment (AKA) questionnaire and determine the relationship between patient anticoagulation control as measured by the international normalized ratio (INR).

Method: The study was a consecutive cross-sectional survey. Patients (n= 70) on warfarin and visiting outpatient clinic of the cardiology unit from July 2016- September 2016 were recruited upon their consent and asked to complete the AKA questionnaire. Demographic and clinical data were manually extracted from patients' record data. Passing score was defined as at least 12 correct responses out of 23- INR relevant AKA questions (52%). INR control was defined by 3 outcome measures: number of INRs within goal range, time in therapeutic range (TTR), and standard deviation (SD) of INR values.

Results: Seventy patients enrolled for this study and 85.7% (n= 60) of the recruited patients consented to participate (females 45%; mean age± SD 60.07±7.75; % with post-secondary education 28.3%). Most patients (n=52) had goal INR ranges of 2.0 to 3.0 (86.6%). Forty-five percent (n= 27) of participants had adequate knowledge of warfarin. There was no significant relationship between number of correct INR-relevant responses and INR control as defined by any of the 3 measures (count of INR values within range rho = 0.070, P = 0.595; TTR rho = 0.092, P = 0.595; and SD rho = 0.118, P = 0.371).

Conclusion: Less than half of the participants had adequate knowledge of warfarin use and there was no significant relationship between patient warfarin knowledge and INR control. However, a more robust multiple centred survey is recommended before generalizability of outcomes.

KEYWORDS: Warfarin knowledge, anticoagulation, INR control

INTRODUCTION

Anticoagulation with warfarin is a well-established and crucial intervention for the prevention and treatment of thromboembolic events.[3] Numerous factors can affect the clinical response of warfarin such as a patient's concurrent disease states, drug regimens, diet and alcohol consumption, physical illness, compliance and overall knowledge of therapy.[4] Furthermore, the maintenance of the therapeutic level of anticoagulation requires a good understanding of the pharmacokinetics and pharmacodynamics of warfarin and good patient communication.[3] There is a consensus in the literature that improved patient knowledge about warfarin therapy improves therapeutic outcomes and the rate of adverse outcomes events is inversely related to the level of their knowledge and literacy skills.[1,5] However, some recent researches reported no association between patient's knowledge of warfarin and anticoagulation therapy.[6] It is therefore important that the level of knowledge of patients about warfarin therapy be evaluated before being prescribed for use.

In a sample of 447 patients attending an anticoagulation clinic, Baker et.al., 2011 found no correlation between patient knowledge on warfarin and INR control defined as the count of 10 previous INR values within goal range (rho = -0.022, p = 0.776), time in therapeutic range (TTR) (rho = 0.015, p = 0.848) and standard deviation of INR values (rho = 0.047, p = 0.047, p =0.550).[8] Similarly, a study carried out by Ahmed 2014, found no relationship between patients' knowledge of warfarin and INR control (OR 1.35, 95 %CI: 0.537 –3.392)[6]

However, a study by Tang et.al, 2003 reported a correlation between patients' warfarin knowledge and the number of INR values that was within the target range in the four most recent clinic visits (r 0.20; p = 0.024).[7] In addition, a study by Kagansky et. al., 2004 stated insufficient education on oral anticoagulation therapy (as perceived by the patient or caregiver) has a significant predictive factor for major bleeding events (5.2 per 1,000 patient-months) compared with the group with no education (1.1 per 1,000 patient-months) and those with sufficient education of oral anticoagulation therapy (0.5 per 1,000 patient-months, p < 0.001). The percentage of INRs within the therapeutic range was highest among patients with perceived satisfactory education (45.1%) compared with those who perceived their education as insufficient (34.9%) or received no education (20.0%, p < 0.001).[2] To date, there is no published research on the evaluation of patients' knowledge on warfarin therapy and INR control using any validated research instrument in Nigeria, hence the reason for this study.

Currently, there are two validated and accepted questionnaires used to measure patient's knowledge of warfarin therapy which are the Oral Anticoagulation Knowledge (OAK) test, developed and validated by Zeolla et al., (2006) [8] and the Anticoagulation Knowledge Assessment (AKA) questionnaire validated by Briggs et. al., (2005)[9].

This study aims at assessing the level of knowledge of warfarin therapy using validated Anticoagulation Knowledge Assessment (AKA) questionnaire in outpatients attending Cardiology clinic of a tertiary hospital and determine the relationship between patient anticoagulation control measured by using number of INRs within therapeutic range, time in therapeutic range (TTR) and standard deviation (SD) of INR values as indicators of control.

METHOD

This was a descriptive survey carried out at the Outpatient clinic of the Department of Internal Medicine, Lagos University Teaching Hospital (LUTH), Idi-Araba, Lagos, Nigeria. The study centre is a tertiary hospital located in Lagos with 761 bed spaces for admission. The study was conducted from July, 2016 to September, 2016. Participants were outpatients who are currently prescribed warfarin and visited the Cardiology clinic during the study period. The study population recruited was 70 however, 85.7% of the recruited sample completed the study (n = 60). A validated questionnaire (Anticoagulation Knowledge Assessment questionnaire by Briggs et al, 2005)[11] which contains 33 questions assessing patients' elementary knowledge of warfarin, its adverse effects and drugs interaction was adapted to suite the Lagos population and pretested to determine its reliability to measure the expected outcomes.

The instrument consisted of two parts; Part A and Part B. Part A consisted of demographic data and Part B was a 24-question AKA test (adapted from 33-question AKA test). Each question was worth 4.35 points. Correctly answering 17 questions (74%) or more was needed for determination of adequate knowledge of anticoagulation therapy (excellent passing score) while correctly answering 12 questions (52%) would show average knowledge (fair passing score). Answering incorrectly or 'I don't know' attracts 0 point. Less than 52% score was seen to show lack of knowledge. The scoring method used was the total count of correct answers for the instrument, with a maximum of 23. Among the total questions in the adapted AKA questionnaire, 16 questions are considered relevant. The scoring method for the relevant questions was correctly answering 12 out of the 16 relevant questions showing excellent (70%) level of knowledge and 8 out of the 16 relevant questions showing average (50%) level of knowledge. Less than 50% score showed lack of knowledge on relevant questions.

Assessment of INR control

To determine the relationship between warfarin knowledge and INR control, the last five INR values obtained prior to the date of patient consent were assessed for evaluation

of a patient's recent INR control at the time of assessment of warfarin knowledge using the AKA instrument. Outcomes measured were numbers of INR within therapeutic range, average time in therapeutic range (TTR) and standard deviation (SD) of INR values using Rosendaal method.

We assessed INR control by calculating the time in therapeutic range for each patient using an adapted linear interpolation method, defined as the proportion of person-time within the target therapeutic range over the total person-time of follow-up.[10] In Rosendaal method the difference between 2 consecutive INR readings, which was within the target range, was divided with the total difference between them. Ethical approval was obtained from Health Research and Ethics Committee, Lagos University Teaching Hospital, Idi-araba, Lagos.

Statistical analysis

Descriptive statistics with counts and percentages were used to illustrate the results. Chi-square test was used to detect if there were any associations between demographic characteristics, knowledge and anticoagulation control. Bivariate analyses of INR control with anticoagulation knowledge were assessed with Spearman's rho correlation, INR control was defined by 3 outcome measures: number of INRs within therapeutic range, time in therapeutic range (TTR) calculated using the Rosendaal method, and standard deviation (SD) of INR values. A p-value of < 0.05 was considered as statically significant. Statistical analyses were conducted using the Statistical Package for Social Science (SPSS) software, version 20.1

RESULTS

Table I: Demographic characteristics of patients
A total of 60 respondents were used for the study. 27 (45%) were females and 33 (55%) were males. The mean age ± SD of the respondents was 60.07±7.75 years and 36.6% (n = 22) diagnosed of atrial fibrillation

CHARACTERISTICS	FREQUENCY	PERCENT	P-VALUE
Age			0.552
Mean±SD=60.07±7.75	N=60		
Below 50	13	21.7%	
50-59	16	26.7%	
60-69	16	26.7%	
Above 70	15	25.0%	
Gender			
Male	33	55.0%	0.670
Female	27	45.0%	
INR goal			
2.0-3.0	51	85.0%	
2.5-3.5	9	15.0%	
Level of education			
None	3	5.0%	0.818
Primary	6	10.0%	
Secondary	17	28.0%	
Post-secondary	34	56.7%	

Duration of use of warfarin			p-value
Less than 1 year	20	33.3%	*0.043
1-3 years	21	35.0%	
3-5 years	13	21.7%	
Greater than 5 years	6	10.0%	
Indication for use of warfarin			
Atrial fibrillation	22	36.7%	0.311
Deep vein thrombosis	12	20.0%	
Cerebral vascular accident	9	15.0%	
Transient ischemic attack	4	6.7%	
Valve replacement	3	5.0%	
Pulmonary embolism	8	13.3%	
Others	2	3.3%	

*indicates significance as p-value< 0.05

Knowledge of Warfarin therapy

Tables IIa and IIb shows that 34 patients (56.7%) lacked adequate knowledge on all the questions in the AKA questionnaire by scoring below average of the total score (< 52%) and half of the participants (50%) lacked adequate knowledge on the relevant questions on warfarin therapy asked, while 27 (45%) patients had average knowledge on warfarin therapy.

Table IIa: Patients' knowledge of all questions in AKA questionnaire.

Level of Knowledge	Frequency	Percent
Excellent	1	1.7%
Average	25	41.7%
Fail	34	56.7%

Table IIb: Knowledge based on relevant warfarin therapy questions

Level of Knowledge	Frequency	Percent
Excellent	3	5.0%
Average	27	45.0%
Inadequate	30	50.0%

Table IIc : Frequently missed/correct questions

Question	Answered Correctly	Answered Wrongly
#21 how warfarin works	51.7%	48.3%
#10 frequency of INR test recommended	26.7%	73.3%
#7 amount of vegetable recommended while on warfarin therapy	20%	80%
#21 where warfarin works	6.7%	93.3%
#15 effect of alcohol on INR	5%	95%

Table III: Correlation between INR values, Time in therapeutic range and Co-morbidity.

TTR and INR values within goal range:	(rho = 0.755; *p = 0.000).
Co-morbidity and INR values within goal range	(rho = - 0.332; *p = 0.023)
Co-morbidity and TTR	(rho = - 0.325; *p = 0.026)

*indicates significance as p-value< 0.05

Table IV: Correlation between Knowledge and INR control

	Number of INR values within goal	Time in Therapeutic range	Standard Deviation range
	Spearman's Rho	Spearman's Rho	Spearman's Rho
	(p)	(p)	(p)
Total AKA score	-0.030 (0.818)	0.022 (0.869)	0.161 (0.220)
INR-relevant AKA items	0.070 (0.595)	0.092 (0.485)	0.118 (0.371)

DISCUSSION

This study was aimed at assessing the knowledge of patients receiving warfarin by using Anticoagulation Knowledge Assessment (AKA) questionnaire and to determine relationship between patients' knowledge of warfarin and INR control (i.e. number of INRs within therapeutic range, time in therapeutic range (TTR) and standard deviation (SD) of INR values) among outpatients attending cardiology clinic of Lagos University Teaching Hospital (LUTH).

The result on the knowledge of warfarin by respondents, showed that only one (1.7%) participant had an excellent knowledge of warfarin - related questions (74%) however half of the respondents had adequate knowledge of warfarin based on the total number of corrected answers on warfarin-relevant questions. Of all those who had adequate knowledge, 66.7% had post-secondary education, although the p-value showed no statistically significant association between literacy and warfarin knowledge (p = 0.818). This result agrees with outcomes of a study from

North Africa where study participants who had a type of formal education recorded the high scores and level of education was reported to be statistically associated with patient's knowledge of warfarin.[11] In this study, no statistically association was found between patients' knowledge of warfarin, gender, age and indication for use respectively. (p = 0.552; 0.672 and 0.311). However, the knowledge of patients was significantly associated with increase duration of use of warfarin (p= 0.043). Thus, it can be inferred that as years go by, patients on long term warfarin medication acquire education about anticoagulants. This outcome supports a study by Baker et al, which reported an association between duration of warfarin use by patients and adequate knowledge on anticoagulants using the AKA questionnaire.[6]

More than half of the respondents' recorded wrong answers in areas of warfarin mechanism of action of warfarin need for laboratory monitoring, diet and lifestyle. There is therefore a need for counselling of long term warfarin users in the highlighted areas in order to prevent

probably adverse reactions due to misuse of warfarin. Similarly, a previous study conducted in the U.S highlighted similar deficient areas.[6]

Furthermore, in the correlation analysis, there was an association between presence of co-morbid diseases and INR control (p= 0.023). This finding is consistent with literature as INR, which is a surrogate clinical parameter, is affected by numerous clinical factors among which is the presence of concurrent disease states.[12-13]

INR control was measured by 3 outcomes: Number of INR values within goal range, time in therapeutic range (TTR), standard deviation (SD). Several studies have provided strong evidence of a link between TTR and these definitive outcomes[14-16].The most direct evidence for TTR as a predictor of adverse events comes from a study that divided patients into three groups by TTR:< 60%, 60%–75%, and >75%[17-18]. The second method involved the number of visits where the INR reading was within the range divided by total number of visits.[18]

There was a strong association between TTR and INR values within goal range ((rho = 0.755; P = 0.000). This infers that TTR and INR are directly proportional and time in therapeutic range (TTR) is a good measure for INR control. However, there was no correlation between patient warfarin knowledge and INR control and this study outcome is similar with results of some previous surveys.[6-7]

Study limitation

This study is limited by its cross-sectional nature but it does not rely only on data acquired by questionnaire-based interviews, all medical records for interviewed patients were reviewed for specific information. Also, the number of study participants recruited for the study was limited and there is the possibility that patients had different understanding of questions asked due to language barrier. The interview was conducted primarily in English and some study participants lacked adequate understanding of this

language.

CONCLUSION

Findings from the study indicated that less than half of the participants had adequate knowledge of warfarin use and there was no significant relationship between patient warfarin knowledge and INR control. However, a more robust multiple centred survey is recommended before generalizability of outcomes.

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