



Assessment of Anticoagulation Control Association with Warfarin Knowledge and Demographic Features of Iranian Population

Mohammad Esmaeel Zangenehfar¹, Iman Harirforoosh¹, Bahram Mohebbi ² and Zahra Khajali ^{1,*}

¹Rajaie Cardiovasar, Medical and Research Center, Iran University of Medical Sciences, Tehran, Iran

²Cardiovascular Intervention Research Center, Rajaie Cardiovasar, Medical and Research Center, Iran University of Medical Sciences, Tehran, Iran

*Corresponding author: Rajaie Cardiovasar, Medical and Research Center, Iran University of Medical Sciences, Tehran, Iran. Email: khajaliz@yahoo.com

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Abstract

Background: Warfarin is the most commonly used oral anticoagulant for patients with atrial fibrillation, prosthetic heart valves, and deep vein thrombosis with a narrow therapeutic index. Due to the importance of patients' adherence to treatment and also regular measurements of International normalized ratio (INR), this can have a significant impact on the quality of anticoagulation control.

Objectives: The primary aim of this study was to assess the association between warfarin knowledge and time in therapeutic range (TTR) in patients on warfarin anticoagulation for at least 6 months who were referred to anticoagulation clinic in Rajaie Heart Center during 2016 - 2017.

Methods: In this cross-sectional study, 620 patients who had been referred to the outpatient Rajaie Hospital anticoagulant clinic and had been taking warfarin for over six months were asked to fill two questionnaires named anticoagulation knowledge assessment (AKA) during a 12-week period. After obtaining the necessary permits, TTR (by Rosendal method) was calculated using the INR results of patients.

Results: A total of 620 patients completed the questionnaire. The relation between warfarin knowledge and anticoagulation control was not significant. The mean age of the study population was 52.45 SD ± 14.01 years. This study showed a significant relationship between TTR, duration of warfarin usage (PV = 0.03) and the underlying cause of this usage (PV = 0.016).

Conclusions: Prevention of chronic diseases is one of the most important priorities of the health care systems. Reduction in complications such as thrombosis and bleeding can be achieved by efforts to promote patient's knowledge. By recognition of relation between warfarin knowledge and social and demographic indicators, patient's education gap can be detected and also planned for dissolving. This study showed that although many of the patients visited in anticoagulation clinic have poor anticoagulation control, but a major part of them have good knowledge of warfarin usage.

Keywords: Knowledge of Warfarin, Heart Disease, TTR (Time in Therapeutic Range), INR

1. Background

Warfarin is one of the most widely used oral anticoagulants and is administrated for a variety of indications like atrial fibrillation, mechanical prosthetic heart valves, deep vein thrombosis and primary or secondary prevention of arterial or venous thromboembolic events. It has very narrow therapeutic index and the excess use of it is associated with bleeding and in addition, inadequate anticoagulation can cause thromboembolic events. Because of its unique pharmacokinetic properties, achievement of desired result requires regular measurements of the international normalized ratio (INR) to ensure that the patient had received adequate medication dose with the least bleeding risk (1).

The inappropriate use of warfarin results in the risk of bleeding and thrombosis. Warfarin-associated intracranial hemorrhage (2), with 50% mortality rate is one of the most drastic adverse drug events (ADEs). Inadequate anticoagulation causes thromboembolic events and also thrombosis on mechanical valves. Association of patient's warfarin therapy knowledge and their demographic background and therapeutic outcomes were also studied (3-5). A survey done of Hu et al. (4) showed that higher warfarin knowledge scores were related to high family income and also high level of education and self-employment. Barcellona et al. (6) studied the association of warfarin knowledge and anticoagulation control in 219 patients. This study showed a positive relation between acceptable TTR and high warfarin knowledge score. Another survey

in Qatar showed a positive association between warfarin knowledge and INR control in patients with warfarin use (5). In a survey by Davis et al. with an 18-question multiple-choice test, no positive relation between patients' demographic characteristics, warfarin knowledge and anticoagulation control was seen (7).

2. Objectives

The primary aim of our study was evaluation of positive relationship between the knowledge of patients receiving warfarin in the outpatient anticoagulant clinic by using the validated anticoagulation knowledge assessment (AKA) questionnaire and anticoagulant control as measured by the INR. Secondary aims of the study were to evaluate the relation between the patient's warfarin knowledge, anticoagulant control and their demographic information such as age, gender and level of graduation etc.

3. Methods

This cross-sectional prospective survey was processed over a 12-week period in Rajaie Heart Center (RHC) outpatient anticoagulant clinic. This center is a tertiary care hospital in Tehran, Islamic Republic of Iran with at least 700 inpatient bed capacity. All adult patients (≥ 18 years old) who referred to the outpatient anticoagulant clinic for showing the result of INR test who were on anticoagulation therapy for over 6 months were asked to participate in the survey. The exclusion criteria of this study was discontinuation of warfarin usage for more than 5 days during the study time, hospitalization during the survey period for any reason, having an inconclusive questionnaire or not having four consecutive INR readings.

The study objectives were explained and written and informed consent was also obtained from patients. A trained researcher filed the questionnaires in a face-to-face setting and was monitored to ensure the quality of research. The questionnaire consisted of three main parts; patients' demographic information such as age, gender, educational level, occupation, socioeconomic, the place of living and marital status was the first part. Second part included "Warfarin knowledge measurement" by an 8-item survey questionnaire (anticoagulation knowledge assessment (AKA)). Finally, the last part was "assessment of the INR level". The warfarin knowledge questionnaire's subjects were interacted for food-drug; drug-drug; the reason for taking warfarin and the actions that was done probably if there was a missed dose or bleeding occurrence when the patient is on warfarin treatment. The language experts

translated the questionnaire to Persian according to international guidelines. Then the questionnaire was validated in Persian language using a multiple-choice question format by twelve expert cardiologists in three different important universities. In AKA questionnaire each correct answer was given one point. The questionnaire's score was interpreted "good knowledge" when more than 16 correct answers were given by the patient. TTR calculated regarding at least three consecutive INR readings of each patient, on an average of a 12-week period, which were obtained from the electronic data center of hospital laboratory. An appropriate INR for the patients with non-valvular AF, thromboembolic and AVR were between 2 - 3, where the goal of INR control was within the range of 2.5 - 3.5 for MVR and 3 - 4 for mechanical right sided heart valves. A TTR range of more than 70 percent was considered good control, the level between 50 and 70 percent represented intermediate and below 50% considered poor control (8, 9).

3.1. Statistical Analysis

Anticoagulation knowledge level was resolute calculated according to total score of the AKA questionnaire. One point was given for any correct answer and no point was given for wrong answers. Patients who answered as a minimum number of 16 were well-thought-out to have obtained passing score as "good warfarin knowledge".

Data were analyzed by using SPSS (IBM SPSS Statistics for Windows, version 22.0. Armonk, NY: IBM Corp. USA). Results were reported as mean \pm SD, and categorical data were presented as numbers and percentages. The association between TTR and the independent variables (gender, age, duration of warfarin therapy, education level, and AKA questionnaire score) was investigated by spearman correlation. Significance was defined as P-value < 0.05 .

4. Results

4.1. Patients

A total of 620 patients were enrolled in this survey, who had attended the outpatient anticoagulation clinic. The patients' demographic characteristics are summarized in relation to their knowledge and level of anticoagulation control in [Table 1](#).

The mean age of the study population was 52.45 SD \pm 14.01 years. Among the 620 participants, 407 (66%) were female, 400 (64.6%) were aged 50 and above, 37 (6%) were less than 30 years old and 183 (29.3%) between 30 - 50 years old. Also, 29 (4.7%) participants had not had any formal education and 75 (12%) had a university education. One hundred and fifteen of the participants (18.7%) were employees, 22.6 percent had miscellaneous job and the remainder

Table 1. Patients' Basic Information

Variable	No. (%)
Educational state	
Illiterate	29 (4.7)
Primary education	259 (42)
Diploma	257 (41.3)
College education	75 (12)
Total	620 (100)
Employment state	
Employee	115 (18.7)
Miscellaneous jobs	140 (22.6)
Housewife	365 (58)
Total	300 (100)
Duration of Warfarin usage, y	
< 1	112 (18)
1 - 5	131 (21.4)
5 - 10	174 (28)
10 - 20	120 (19.3)
> 20	83 (13.3)
Underlying cause for warfarin usage	
Mitral valve replacement (MVR)	292 (48.7)
Aortic valve replacement (AVR)	41 (6.7)
Tricuspid or Pulmonary valve replacement (TVR/PVR)	41 (6.7)
More than one valve replacement	78 (12.7)
Deep vein thrombosis (DVT)	32 (5.3)
Atrial fibrillation (AF)	94 (15.3)
CABG	20 (3.3)
Pulmonary emboli (PE)	22 (3.5)
Socioeconomic state	
Poor	78 (12.7)
Moderate level	296 (48)
High level	243 (39.3)
Residential location	
Urban	531 (86)
Suburb	89 (14)
Warfarin knowledge	
Poor	6 (1)
Moderate	255 (41)
Good	309 (50)
Very good	50 (8)
Gender	
Female	407 (66)
Male	213 (34)
Age, y	
≤ 30	37 (6)
30 - 50	181 (29.3)
50 - 60	181 (29.3)
> 60	218 (35.4)

were unemployed (Table 1). Majority of the patients had regular follow-up and attendance in the anticoagulation clinic. The minority stated they could not always attend

the clinic. The most common indication for warfarin therapy was Mitral valve replacement (48.7%) followed by atrial fibrillation (15.3%) and replacement of more than one prosthetic heart valves (12.7%) (Table 1). Another information we concluded in our study was the duration of warfarin usage. It is named in Table 1 as the duration of having underlying cause for warfarin usage such as MVR etc.

Additionally, the findings show that about half of the participants (48%) were in moderate socioeconomic state and majority of the patients were urban residents (in Tehran) and the rest of them were resident in suburban locations (Table 1).

Findings indicate that a large percentage of patients (28%) were on warfarin anticoagulation for 5-10 years.

Results of this study also show that most of the precipitants are in good warfarin knowledge category meaning 41.3% were in moderate group and only one percent had poor knowledge about warfarin and its usage issues (Table 1).

Our study showed 43% of patients had acceptable TTR and good control of anticoagulation treatment, 20% had moderate and 37% had poor control INR and TTR (TTR less than 50%). Findings point out that there is no significant relation between TTR and gender ($PV = 0.96$) or age of the precipitants ($PV = 0.256$). Also, no significant relation was seen between TTR and residential location ($PV = 0.798$) or educational ($PV = 0.488$) or employment ($PV = 0.889$) or economic status ($PV = 0.364$) of the patients.

On the other hand, results of this study show a significant relation between TTR and duration of warfarin usage ($PV = 0.03$) and underlying cause of this usage ($PV = 0.016$). The patients who had started warfarin in less than 1 year had better INR control than other subgroups. Moreover, more than half of the patients who were on warfarin anticoagulation in order to prevent thromboembolic events due to Atrial fibrillation or to prevent VTE such as DVT or pulmonary embolism, had a good control of INR. We could not find any significant relation between warfarin knowledge and TTR (Table 2).

5. Discussion

Warfarin therapy for a long period is recommended for many patients such as those with atrial fibrillation who are at risk of stroke or many other cardiovascular problems like those with recurrent venous thrombosis or artificial heart valves (10).

Patients' education before starting warfarin anticoagulation-regarding signs and symptoms of bleeding, the impact of diet on INR control, potential drug interactions and what should be done if one dose is missed are pivotal in successful warfarin usage.

Table 2. The Relation Between TTR and Warfarin Knowledge, Years of Warfarin Usage and Underlying Diseases

	TTR ^a			Kruskal Wallis Exam Result
	Poor Control (0 - 49)	Intermediate Control (50 - 70)	Good Control (70 - 100)	
Warfarin knowledge				P = 0.399 ^b
Poor and moderate	113 (47.4)	46 (36.7)	102 (38.1)	
Good	107 (45.6)	57 (46.7)	145 (55.6)	
Very good	16 (7.0)	18 (16.7)	16 (6.3)	
Total	236 (100)	121 (100)	263 (100)	
Duration of warfarin usage				P = 0.030 ^c
Less than one year	33 (29.6)	20 (18.5)	59 (51.9)	
1 - 5 years	33 (25)	32 (25)	66 (50)	
5 - 10 years	70 (40.5)	20 (11.9)	84 (47.6)	
10 - 20 years	75 (62.1)	20 (17.2)	25 (20.7)	
> 20 years	23 (30)	29 (35)	29 (35)	
Underlying cause of usage				P = 0.016 ^c
AVR/MVR	169 (50)	46 (14)	117 (36)	
PVR/TVR	8 (21)	12 (29)	22 (50)	
Replacement of more than one valve	24 (31.6)	28 (36.8)	26 (32.6)	
Thrombosis prevention	35 (21.1)	35 (21.1)	98 (57.9)	

^a Values are presented as No. (%).

^b There is no significant statistical difference between these groups.

^c There is significant statistical difference between these groups.

This is not the first study of this kind that evaluates the knowledge of warfarin therapy and anticoagulation control (INR) based on patients' demographic characteristics as previous similar studies done in Saudi Arabia can be pointed out. This study was focused on evaluation of the association between educational or socioeconomic status and anticoagulation control within the Iranian population. The results of good INR control range from 14% to 48% in previously published studies in the literature. Davis et al. (7) in their study showed that only 14% of patients who were on warfarin anticoagulation achieved acceptable levels of anticoagulation control, defined as about more than 70% of INR values within therapeutic range. In our study 43% of patients had acceptable level of anticoagulation control.

In this study we found that there is no significant relationship between TTR and gender (PV = 0.96) or age of the participants (PV = 0.256) and no significant relation was noted between TTR and residential location (PV = 0.798) or educational (PV = 0.488) or employment (PV = 0.889) or economic status (PV = 0.364) of the patients.

Results of this study shows significant relation between TTR and duration of warfarin usage (PV = 0.03) or underlying cause of this usage (PV = 0.016); for example,

more than half of the patients who were on warfarin anticoagulation in the hope of preventing thromboembolic events due to atrial fibrillation or preventing VTE such as DVT or pulmonary embolism, had good control of INR.

Despite the fact that major part of our patients had good knowledge of warfarin and also good health literacy, significant percentage did not have good control of INR, and we could not find a significant relationship between acceptable TTR, warfarin knowledge and health literacy.

Safety and effectiveness of warfarin anticoagulation is very important in overall management of the patients. TTR would be helpful for achieving this purpose, and it is also a way of summarizing the INR control over time.

5.1. Limitations of the Study

Our study has the following limitations: (1) our sample did not show a whole group of patients such as people at local and poor economic area, so larger multi-centered studies should be done and then meta-analysis and systematic review of these studies would be necessary for precise conclusion about this matter; and (2) we could not include the all aspects that affect INR variation like diets, herbal medications and/or dietary supplements and this could have a negative impact on the final conclusion.

5.2. Conclusions

This study showed that although many of the patients who had visited in the anticoagulation clinic have poor and moderate but not good anticoagulation control, a major part of them have good warfarin knowledge. There was no significant relationship between warfarin knowledge and anticoagulation control. Larger studies should be done for evaluation of association between adequate adherence of warfarin therapy and anticoagulation control. Multi-centered; meta-analysis or systematic review studies of data are also needed for the final conclusion.

Footnotes

Authors' Contribution: ZK and MEZ contributed to the design and implementation of the research to the analysis of the results. BM and IH contributed to the writing of the manuscript.

Conflict of Interests: The authors declare that they have no competing interests.

Ethical Approval: study design and protocols were approved by the Ethics Committee of the Research Deputyship in Rajaie Cardiovascular, Medical and Research Center (ID: IR.RHC.REC.1395.027).

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