Satisfaction with Warfarin Therapy and It's Relation with International Normalized Ratio Monitoring

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Abstract—Background: Use of oral anticoagulant therapy (OAT) has been associated with reduction in morbidity and mortality of thromboembolic complications. The use of vitamin K antagonist is effective in the prevention of thromboembolic complications. However, its use also implies lifestyle modifications and change in the behavior which may affect in a negative way patient's quality of life. Warfarin is the most frequently used oral anticoagulant. Satisfaction was associated significantly with better control of INR, which in turn is critical in evolving educational interventions for a better patient care. Treatment with warfarin requires proper and regular monitoring to prevent the thromboembolic complications as well as to prevent over anticoagulation state. This study aimed to assess satisfaction level among warfarin patients as well as to evaluate factors influencing their level of satisfaction. Methods: A prospective observational cross-sectional study was conducted on 133 patients during a period of six weeks: (from 24th of December 2018 till 29th of January 2019) at the Anticoagulation Clinic at Queen Alia Heart Institute, who were on warfarin therapy using the validated Anti-Clot Treatment Scale (ACTS). Results: Among 133 patients who completed the questionnaire, the majority of patients (52.63%) were considered dissatisfied with their treatment with total frequency of seventy patients, while fifty five patients (41.35%) were considered satisfied with it. Female patients, those who live outside Amman, and patients who experienced a previous bleeding episode, were more dissatisfied with their treatment. While Non-smoker patients, and those who have a higher monthly income were more satisfied with their treatment. Conclusion: This observational study called for urgent strategies to improve the satisfaction degree in warfarin patients; one of the factors that are important determinant of better INR control. Thus, it is a must to apply methods of best practice to enhance the satisfaction by the following probable solutions; opening anticoagulant clinics in peripheral hospitals provided with clinical pharmacist as well as dietitian in order to reduce the burden on patients to visit the capital city, maintenance and monitoring the (INR) to be within the optimal therapeutic target range in order to reduce the possibility of bleeding episodes, and encourage the patients who are smoking to quit it at every possible visit to the clinic.

Keywords— INR, Oral anticoagulant therapy, Satisfaction, Warfarin.

I. INTRODUCTION

Thrombosis is responsible for about one in every four deaths worldwide, and it is a considerable contributor in universal disease burden and death-rate (Sonuga, et al., 2016). Oral anticoagulants therapy is influenced by: co-administered drugs, anticoagulation intensity, physician's experience, laboratory testing, patient's compliance, and their educational level (Joshua, and Kakkar, 2015). Universally, management of anticoagulant therapy is a big challenge for laboratory and clinical services (Sonuga, et al., 2016). Warfarin is a widely used oral anticoagulant. Satisfaction with anticoagulant therapy is a significant issue, which will impact patients' clinical outcomes (Geng, et al., 2018). Burden of anticoagulant therapy affects patient's satisfaction, which in turn affects treatment adherence (Okumura, et al., 2018). Satisfaction with oral anticoagulant therapy is an important factor that decreases mortality and morbidity (Eltayeb, et al., 2017). Good control of INR was associated strongly with higher patient's satisfaction with anticoagulation. While dissatisfaction with warfarin therapy lead to poorer control of INR and poorer clinical consequences (Balkhi, et al., 2018).

Warfarin use requires a close monitoring if used on long-term basis in an outpatient settings (Shrestha, et al., 2015). Because most patients respond differently to warfarin dose, under-coagulation may lead to an increased hazard level of clot formation. While over-coagulation may lead to increased hazard level from excessive bleeding (Mahtani, et al., 2014).

II. METHODS

Design

A prospective observational cross-sectional study was carried out at the Anticoagulation Clinic at Queen Alia Heart Institute (QAHI), at King Hussein Medical Center (KHMC). This clinic was established for the monitoring of patients on anticoagulation therapy.

Ethical considerations

The study was approved by the scientific committee of the School of Pharmacy, as well as the School of Postgraduate Studies at the University of Jordan. Ethical approval was obtained from the ethics committee at Royal Medical Services (RMS) to perform it at QAHI.

Participants

The study included adult patients (18-years-old or older), who were receiving warfarin therapy for any clinical indication for at least four months (16 weeks) prior to enrolment. Each patient had at least four previous INR readings in the medical records for the last sixteen weeks and gave verbal consent to participate. Patients incapable of communicating verbally or who refused to give consent were excluded from the study.

Instrument and Data collection

The second part of questionnaire measured patient's satisfaction with warfarin treatment using seventeen items Anti Clot Treatment Scale (ACTS) (Balkhi, et al., 2018). Questionnaire included two subscales to measure benefits and burdens of Anti Clot Treatment (ACT). Benefit subscale which contains four items subscale (three items and a global question regarding positive impact for ACT on patient's life). Burden subscale contains thirteen items (twelve items and a global question regarding negative impact for ACT on patient's life). The patients were asked to rate their experiences with anticoagulants therapy during past four weeks on a five points intensity scale, corresponding as: one: Not at- all, two: A little, three: Moderately, four: Quite a bit, five: Extremely.

The higher the score is the higher the dissatisfaction level is. While, in calculation process for benefit subscale, greater scores indicates higher satisfaction, while lower scores indicates higher dissatisfaction. In the procedure of interpretation for ACT scores the patients were categorized into two groups, satisfied or dissatisfied according to the scores of burden and benefit subscales. If the score of burden subscale was greater than score of benefit subscale, the patient was considered dissatisfied, while if the score of burden subscale was smaller than score of benefit subscale the patient was considered satisfied.

The following definitions were adopted throughout the follow up of patients. INR stability or INR control is the percent of number times INR readings was optimal over the number of times it was measured. The "safe warfarin management" approach is when stability of INRs, greater than or equal to fifty percent, which means an INR in an optimal ranges more than half tested times, (Shilbayeh, et al., 2018).

The "Good control" of INR had been defined by Time in Therapeutic Range (TTR), calculated using Rosendaal method. A TTR greater than seventy five percent was considered controlled (Rosendaal, et al., 1993). In the procedure of interpretation for TTR score data we categorized our patients into three groups: un-safe warfarin management, safe warfarin management, or safe warfarin management with good control.

Statistical analysis

Data were coded, entered and analyzed using IBM Statistical Package for Social Sciences (IBM SPSS®, Version 22). The Non parametric test was used if the data were not normally distributed. The Normality of the data was determined by Shapiro-Wilk test with P-value > 0.05 indicating a normally distributed continuous variable. Descriptive statistics were used to describe patient's characteristics. Categorical data were reported as frequencies and percentages. Continuous data were reported as mean ± standard deviation (SD) or median and interquartile range (IQR) as appropriate. Responses to each item in the questionnaire was expressed as frequencies and corresponding percentages. When comparing baseline variables the non-parametric statistical tests were used accordingly. Mann–Whitney, Kruskal–Wallis H, Pearson Chi square tests.

Individuals who were more satisfied with warfarin therapy were expected to be positively associated and to have a better anticoagulation control status. Correlation between satisfaction scores, and INR control parameter was assessed using bivariate analysis by Chi square tests. A P-value of less than 0.05 was considered statistically significant.

III.   RESULTS

One hundred sixty four patients were invited to participate in our study. From them One hundred forty three patients accepted to participate, with a response rate of 87.2%. Out of these 143 one hundred thirty three patients were included with a drop-out rate of 7.0%. The demographic data and clinical characteristics of the study participants are presented in (Tables 1, and 2). More than two thirds of patients included in the study came from the capital city Amman. More females were included and patients income was mostly middle to low.

TABLE 1: Demographic Data

Characteristics	N (%)
Place of residence	
Capital city	**89(66.9)**
Outside the capital city	**44(33.1)**
Age	
(18-35) years	**17(12.7)**
(36-53) years	**40(29.9)**
(54-71) years	**55(41.0)**
>71years	**20(14.9)**
Educational level	
Low (non- educated/ primary)	**26(19.5)**
Middle (12-18 years of education)	**77(57.9)**
High (> 18 years of education)	**30(22.6)**
Gender	
Female	**83(62.4)**
Male	**50(37.6)**
Insurance	
Exemption*	**61(45.9)**
Military	**72(54.1)**
Marital status	
Single	**15(11.3)**
Married	**89(66.9)**
Other	**29(21.8)**
Monthly Income (JOD)	
Low (0 - 249)	**82(61.7)**
Middle (250 - 500)	**33(24.8)**
High (>500)	**18(13.5)**
Nationality	
Jordanian	**118(88.7)**
Others **	**15(11.3)**

*: Either patients had an endorsement form from the Royal Court or they paid instead of the service.
**: one Syrian, and the remaining were Palestinians.

Answers to benefit subscale are shown in Table 3. The majority of patients had positive responses regarding the benefits of warfarin, with the lowest positive response regarding the overall positive impact warfarin treatment had on their life.

Among 133 patients who completed the questionnaire the median [IQR] benefits subscale was 20.00 [0-20], while the mean ± standard deviation for it was 18.1 ± 3.57. The median [IQR] burdens subscale 20.00 [11-57], while the mean ± standard deviation for it was 22.0 ± 8.90.

Predictors for Satisfaction were the following: place of residence, gender, monthly income, bleeding history, and smoking status ($p < 0.05$), see Table 5 for details.

TABLE 2: Clinical Characteristics

Characteristics	N (%)	
Major bleeding history of patients*		
Negative	**105(78.9)**	
Positive	**28(21.1)**	
Concurrent medical conditions		
None	**67(50.4)**	
DM and/or HTN	**50(37.6)**	
Other£	**16(12.0)**	
Indication for warfarin use		
AF	**49(36.8)**	
AVR	**34(25.6)**	
MVR	**45(33.8)**	
Other€	**5(3.8)**	
Smoking status		
None	**117(88.0)**	
Yes	**16(12.0)**	

DM: Diabetes mellitus, HTN: Hypertension, AF: Atrial fibrillation, AVR: Aortic valve replacement, MVR: Mitral valve replacement
: within the previous four months to enrollment
£: Asthma, Benign Prostatic Hypertension, Coronary Artery Disease, Coronary Heart Disease, Chronic Kidney Disease, Colon cancer, Dyslipidemia, Gout, Hepatitis C, Hyper and hypothyroidism, Migraine, Neurodisorders, Osteoarthritis, Osteoporosis, Pulmonary Embolism, Ulcerative colitis, and Vascular Heart Disease.
€: Antiphospholipid Syndrome, Deep Vein Thrombosis, Senning, and Thrombophilia.

TABLE 3: Benefit Subscale

	N (%)				
	Not at- all	A little	Moderately	Quite a bit	Extremely
1. How confident are you that your anti-clot treatment will protect your health?*	**4 (3.0)**	**1 (0.8)**	**5 (3.8)**	**5 (3.8)**	117 (88.0)
2. How reassured do you feel because of your anti-clot treatment?*	**5 (3.8)**	**3 (2.3)**	**2 (1.5)**	**8 (6.0)**	114 (85.7)
3. How satisfied are you with your anti-clot treatment?*	**6 (4.5)**	**3 (2.3)**	**3 (2.3)**	**5 (3.8)**	115 (86.5)
4. Overall, how much of a positive impact has your anti-clot treatment had on your life?*	**21 (15.8)**	**0**	**12 (9.0)**	**4 (3.0)**	95 (71.4)

*: One Nil value

TABLE 4: Burden Subscale

	N (%)				
	Not at- all	A little	Moderately	Quite a bit	Extremely
1. How much does the possibility of bleeding as a result of your anti-clot treatment limit you from doing physical activity?*	**116 (87.2)**	**4 (3.0)**	**6(4.5)**	**0**	6 (4.5)
2. How much does the possibility of bleeding as a result of your anti-clot treatment limit you from taking part in your usual activities?*	**114 (85.7)**	**2 (1.5)**	**8 (6.0)**	**0**	8 (6.0)
3. How bothered are you by the possibility of bruising as a result of your anti-clot treatment?	**91 (68.4)**	**6 (4.5)**	**19 (14.3)**	**3 (2.3)**	14 (10.5)
4. How bothered are you by having to avoid other medicines as a result of your anti-clot treatment?	**89 (66.9)**	**4 (3.0)**	**15 (11.3)**	**3 (2.3)**	22 (16.5)
5. How much does your anti-clot treatment limit what you eat and drink?	**90 (67.7)**	**3 (2.3)**	**17 (12.8)**	**3 (2.3)**	20 (15.0)
6. How much of a hassle are the daily aspects of your anti-clot treatment?	**105 (78.9)**	**5 (3.8)**	**8 (6.0)**	**3 (2.3)**	12 (9.0)
7. How much of a hassle (inconvenience) are the occasional aspects of your anti-clot treatment?	**81 (60.9)**	**6 (4.5)**	**16 (12.0)**	**6 (4.5)**	24 (18.0)
8. How difficult is it to follow your anti-clot treatment?	**76 (57.1)**	**16 (12.0)**	**20 (15.0)**	**2 (1.5)**	19 (14.3)
9. How time-consuming is your anti-clot treatment?	**126 (94.7)**	**3 (2.3)**	**1 (0.8)**	**0**	3 (2.3)
10. How much do you worry about your anti-clot treatment?	**95 (71.4)**	**4 (3.0)**	**10 (7.5)**	**9 (6.8)**	15 (11.3)
11. How frustrating is your anti-clot treatment?	**111 (83.5)**	**4 (3.0)**	**5 (3.8)**	**2 (1.5)**	11 (8.3)
12. How much of a burden is your anti-clot treatment?	**92 (69.2)**	**7 (5.3)**	**12 (9.0)**	**2 (1.5)**	20 (15.0)
13. Overall, how much of a negative impact has your anti-clot treatment had on your life?*	**109 (82.0)**	**0**	**11 (8.3)**	**3 (2.3)**	9 (6.8)

TABLE 5: Predictors for Satisfaction*

Characteristics	Benefit: Median (IQR)	P-value	Burden: Median (IQR)	P-value
Place of residence				
Capital city			18.50 (9)	
Outside the capital city			23.50 (16)	0.013
Gender				
Female			21.00 (11)	
Male			18.00 (10)	0.024
Monthly Income				
Low	20.00 (2)			
Middle	20.00 (4)	0.051		
High	20.00 (8)			
Bleeding history of patients				
Negative			19.00 (11)	
Positive			23.00 (14)	0.029
Smoking status				
None	20.00 (3)			
Yes	18.00 (4)	0.027		

*: using Mann–Whitney, Kruskal–Wallis H tests, significant at the 0.05 level .

INR Control Parameter Score

The median [IQR] INR control parameter of the study population was 50.00 [0-100], while the mean ± standard deviation for it was 58.8 ± 28.9. Among 133 patients who completed the questionnaire, the majority of patients (48.12%) had a good control with safe warfarin management with total frequency of 64 patients, while 35 patients (26.32%) had a safe warfarin management. While 34 patients (25.56%) had un-safe warfarin management.

The majority of participants (74.4%) were having a safe warfarin management.

Relationship between INR Control Parameter and Satisfaction Score

Patients who had a higher ACT scores had a higher INR control parameter scores, and those with lower ACT scores had also a lower INR control parameter scores (Table 6).

TABLE 6: Relationship between INR Control Parameter and Satisfaction Score*

INR control	Satisfied	Dissatisfied	Neutral	Pearson Chi-Square
un- safe warfarin management	19	12	3	
safe warfarin management	18	16	1	0.809
safe warfarin management/ Good control	33	27	4	

*: using Chi square test, significant at the 0.05 level.

IV. Discussion

Satisfaction Score:

This result of this study are in agreement with study that was conducted by Elbur, et al. (2015), in which 57.3% of patients considered the therapy of anticoagulation constitute a burden on them (Elbur, et al., 2015). In contrast, another study done by Eltayeb, et al. (2017) showed that 50.5% of patients were considered as satisfied with their antic lot treatment (Eltayeb, et al., 2017).

Patient- perceived limitations in the following fields: feelings of inconvenience of occasional aspects of thromboprophylaxis therapy, limitations on other medicines, and limitations on diet. This result is in agreement with study that was conducted by Pandya, and Bajorek. (2017), which reported that factors affecting the daily lives of patients negatively, includes: dose adjustments, dietary considerations, and regular therapeutic monitoring for the medication (Pandya, and Bajorek, 2017).

Gender is another factor that could affect burden score. In this study females were more dissatisfied with treatment. This research's result agreed with Fernández, et al. (2018), results from the study shown that, one of the perceived burdens in anticoagulation therapy is gender, since men had a lower level of burden in their treatment (Fernández, et al., 2018). Patients with higher income were more satisfied with treatment. agreed with Eltayeb, et al. (2017), results from the study that showed that, patients who were working at the time of study were more satisfied with warfarin by three times approximately, relative to those without jobs, (OR =2.9, 95%CI= (1.1-7.6), P = 0.035) (Eltayeb, et al., 2017).

Female patients were more dissatisfied than male patients. This research's result agreed with Fernández, et al. (2018), results from the study shown that, one of the perceived burdens in anticoagulation therapy is gender, since men had a lower level of burden in their treatment (Fernández, et al., 2018). Mover, patients having a higher monthly income were more satisfied than patients having a lower monthly income (Table 5). This research's result agreed with Eltayeb, et al. (2017), results from the study shown that, patients who were working at the time of study were more satisfied with warfarin by three times approximately, relative to those without jobs, (OR =2.9, 95%CI= (1.1-7.6), P = 0.035) (Eltayeb, et al., 2017).

Having an episode of bleeding have a negative impact on patient's satisfaction with anicogulant therapy. Indeed, in this study patients who had a positive history of bleeding were more dissatisfied than those who had not. This research's result agreed with previous reports were patients had satisfaction scores decreased after bleeding episode (Kooistra, et al., 2016).

V. Conclusion

This observational study called for urgent strategies to improve the satisfaction degree in warfarin patients; one of the factors that are important determinant of better INR control. Thus, it is a must to apply methods of best practice to enhance the satisfaction by the following probable solutions; opening anticoagulant clinics in peripheral hospitals provided with clinical pharmacist as well as dietitian in order to reduce the burden on patients to visit the capital city, maintenance and monitoring the (INR) to be within the optimal therapeutic target range in order to reduce the possibility of bleeding episodes, and encourage the patients who are smoking to quit it at every possible visit to the clinic.

Limitations:

The study was conducted during a six weeks period. Thus if more time was allotted, more participants may have provided responses. Also, the study was conducted at single unit that cares only for outpatients, it patients might not be representative for all patients in Jordan. Despite that since 1941 the Royal Medical Services provides medical therapeutic services and health services for one third of the kingdom's population, military and civilian, as well as patients from neighboring countries. . Lastly, one of the limitations of the questionnaire part of the study was our choice to use the anti-clot scale with two dimensions; benefit and burden to measure patient satisfaction with warfarin, which was limited by the lack of standardized tools. In order to decrease this, we had done the interpretation for the results separating between benefit and burden subscales.

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