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Research Article

Anticoagulation Therapy: For Patients Attitude, Knowledge and Concerns Regarding their Effects on International Normalized Ratios in Saudi Arabia

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Abstract

Background and Objective: Thoughtful evaluation of patients' knowledge, satisfaction and concerns in anticoagulation clinics helps to understand areas of improvement. This study aimed to examine patients' drug knowledge, satisfaction and concerns with provided anticoagulation services. **Materials and Methods:** This study was designed as a cross-sectional survey that was developed and conducted in a regional anticoagulation clinic with good number of patients. Two hundred sixty eight were recruited in the survey. Patients' warfarin refill records and time within the therapeutic INR range were retrieved from hospital databases. All statistical assessment and analysis were carried out with SPSS. **Results:** Adequate knowledge of warfarin-food and warfarin-drug interactions was lacking in about 50% of patients. Satisfaction with provided service was not optimal. Concerns associated with warfarin was bothersome to many patients due to possible drug-drug interactions (41.42%), missed doses impact (29.10%), adverse drug reactions (29.85%). All of which might lead to unfavorable consequences. Higher satisfaction was associated with better knowledge ($r = 0.27, p = 0.001$) and fewer concerns ($r_s = -0.26, p = 0.002$). Improved drug-related knowledge and higher satisfaction were positively reflected in these patients' attitude toward drug use compliance in knowledge ($r_s = 0.23, p = 0.01$) and satisfaction ($r_s = 0.19, p = 0.041$). Eventually, good INR control was shown more with better knowledge, higher satisfaction and better warfarin adherence ($p = 0.004, 0.03, 0.04$ and 0.004 , respectively). **Conclusion:** There is a deficit in patients' knowledge and satisfaction with warfarin therapy. Such deficits lifted the threshold of concerns with warfarin use and negatively affected INR control.

Key words: Warfarin therapy, international normalized ratio, drug knowledge, anticoagulation services, thromboembolic events

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Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Chronic anticoagulation management for thromboembolic events is mainly achieved by oral warfarin therapy for decades. This is attributed mainly to its ability to alter the coagulation cascade therefore improves the international normalized ratio (INR) in order to prevent further clot formation in patient experiencing higher risk¹. INR being above the normal levels might produce hemorrhage if excessive, whereas low INR values might put patients at risk of additional clotting events²⁻⁴. Warfarin, therefore, must be used with tight follow up to keep INR values within the desirable levels.

Achieving anticoagulation effect after warfarin administration is a multifactorial process. Inter-individual response to the drug varies due to presence of genetic sequence variant that may require several dose changes throughout the course of therapy to obtain steady INR levels⁵. Patient counseling and education will improve response to INR, therefore, achieving desired outcomes. Several studies was able to confirm that better patient awareness of their therapy will eventually improve outcomes (good INR control)^{6,7}. Therefore, obtaining complete patient information is crucial for assessing lack of warfarin knowledge and patient's satisfaction with therapy that shown to worsen medication compliance and compromise INR control. By understanding the deficits and areas of required improvement, intended interventions can be formulated then implemented in overall patient care.

This study was conducted to recognize patients' knowledge and satisfaction with warfarin therapy. The second aim was to evaluate their effect on INR control in Saudi Arabian patients.

MATERIALS AND METHODS

Patient recruitment and data collection: This study was a cross-sectional survey of patients prescribed warfarin for the management of thromboembolic events (chronic use) at a busy regional anticoagulation clinic. The survey was conducted for a period of 6 months (December 2016-May 2017). For a study power of 0.80, it was aimed to recruit at least 253 patients. All patients were adults, male or female, able to read, on warfarin therapy for any thromboembolic event and signed the consent form to participate. The study was approved by ethical committee prior to commencement. Adherence to therapy was obtained from available health information system (HIS) database (pharmacy module) which was reviewed for the past 9 months for doses, supplied quantities and refill regularity in addition to patients'

responses to questionnaire. Warfarin adherence then was computed by refill compliance rate "RCR" from the formula [(sum of quantity dispensed over interval/quantity to be taken/day) × 100]/number of days in interval between first and last refill⁸. For INR control history as being 90% or higher of the time in target therapeutic range, we reviewed the medical laboratory module database in the HIS.

Survey questionnaire: Several questionnaires were reviewed and developed on the bases of previous publications⁹⁻¹¹. In addition to available patient counseling materials that are usually provided to the new patients in the anticoagulation clinic, we developed and used a four step questionnaire that is detailed in the supplementary materials (Warfarin Questionnaire.docx). Briefly, step one included the patients' demographics and characteristics, step two involved questions on patients' knowledge of warfarin therapy, step three composed of a satisfaction scale regarding the care and services in the anticoagulation clinic and step four was a 10 points of concerns regarding warfarin therapy. Before commencing the study, expert opinions and potential patients comments were obtained on the formulated questionnaire and taken in consideration.

Statistical analysis: All statistical assessment and analysis were carried out with IBM SPSS 24.0 (SPSS Inc., Chicago, IL). Data were stated as percentage or Mean ± SD as appropriate. Independent samples t-test, Pearson's Chi-Square test and Mann Whitney U test were used as required. Pearson's or Spearman's correlation analysis was also used to evaluate the correlation between drug therapy concerns with knowledge and satisfaction with the service scores. Same analyses were applied to examine the correlation of warfarin refill regularity with drug knowledge, service satisfaction and drug use concerns scores. Significance was defined by a p value < 0.05.

RESULTS

Demographic data: Survey questionnaire was introduced to around 320 subjects. Only 268 accepted to participate (83.8%). Table 1 and Fig. 1 illustrates study subjects individual

Table 1: Demographic data and patient characteristics

Characteristics	Respondents	
	(n = 268)	(%)
Within target INR in the past 3 months		
<90 (%)	181	67.54%
≥90 (%)	87	32.46%
*Age (years)	55.03	8.85
**Duration for taking warfarin (years)	5.3	4.9

*,** Values are expressed as Mean ± SD

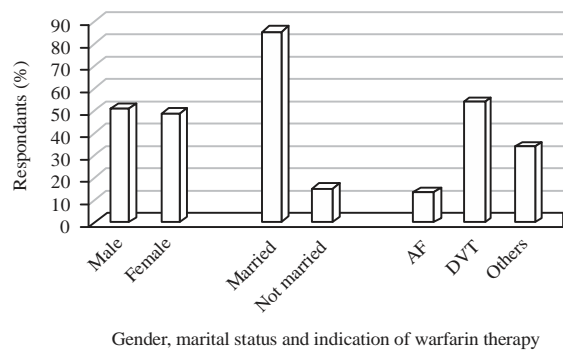


Fig. 1: Percent distribution of gender, marital status and indication of warfarin therapy among the respondents

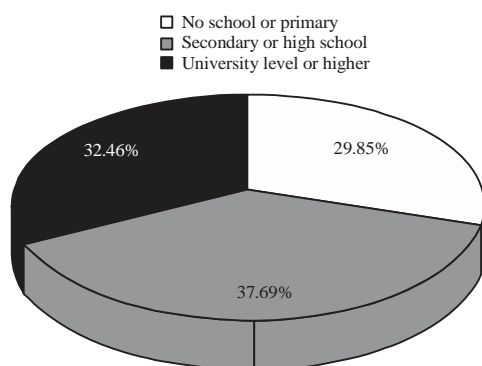


Fig. 2: Percent distribution of educational level among the respondents

differences. Male and females were almost equal among all respondents (51.12% vs. 48.88%, respectively). Patients had a Mean \pm SD age of 55.03 ± 8.85 years. It was noted that patients respondent with inadequate INR control (less than 90%) included 67.54%. More than one third (37.69%) of respondent had secondary or high educational level (Fig. 2). Warfarin refill regularity Mean \pm SD of $90.0 \pm 17.8\%$.

Patient awareness of bleeding as the main warfarin's adverse effect reached 75%, however, fewer patients (55.97%) monitored signs of bleeding. Only about 50% of patients had the knowledge about the relation between warfarin dosage, INR target and treatment complications. About one third of patients were aware about the impact of warfarin on IM injection. As regard warfarin administration, about 70% of patient were aware of warfarin administration. Only about 50% of patient had the knowledge regarding warfarin drug and food interactions (Table 2).

Patient satisfaction with the provided service was Mean \pm SD score of 20 ± 3.37 . Notably, about 95% of surveyed patients felt happy with care providers and 49.6% of patients were not satisfied about the provided service when it comes

to waiting time to see care provider. Table 3 illustrates all given response in this domain.

It was obvious and expected to have more concerns about warfarin therapy regarding drug-drug interactions (41.42%), drug-diet interaction (26.12%) and the side effect of warfarin (29.85%). However low patients' concerns regarding the impact of warfarin therapy on work, the restriction of usual activities and difficulty in following warfarin instructions. All results in this category were shown in Fig. 3.

It is worth mentioning that educated patients and elderlies gave favorable responses in satisfaction related questions, drug related knowledge ($r = 0.27$, $p = 0.001$) and drug use concerns ($r_s = -0.26$, $p = 0.002$). This was positively reflected in these patients attitude towards drug use compliance in both categories (knowledge $r_s = 0.23$, $p = 0.01$ and satisfaction $r_s = 0.19$, $p = 0.041$). Eventually, good INR control was shown more with better knowledge, higher satisfaction, fewer concerns and better warfarin adherence ($p = 0.004, 0.03, 0.04$ and 0.004 , respectively).

DISCUSSION

This study confirmed that many warfarin patients even those of chronic use are not likely to have more than moderate knowledge about the drug. It was also noted that our patients' knowledge deficit was not too much different from other patients in published studies as Davis *et al.*¹² study that reported poor anticoagulant control, knowledge and compliance to warfarin therapy. Knowledge deficit was mainly in warfarin associated food and drug interactions. As it is known about warfarin precautions, its effect will change depending on patient food intake and other medication use^{13,14}.

Similarly, less educated patients and those ranked in upper age groups had less (poor) knowledge on warfarin therapy that affect the desired outcome. This finding was also shown in previously published paper that demonstrated old age as a significant factor underlying poor anticoagulant knowledge⁷. Many factors might have played a role in this trend but could be attributed to cognitive limitations despite educational programs and distributed materials for all new warfarin treated patients. It was believed that more anticoagulation clinic staff must have a positive response from patients to confirm their comprehension of any given instructions. In addition, it would also be recommended to schedule older patients for general warfarin session periodically in order to improve their knowledge on their treatment goals. Use of various educational methods, e.g., audiovisual materials or special educators, could yield a

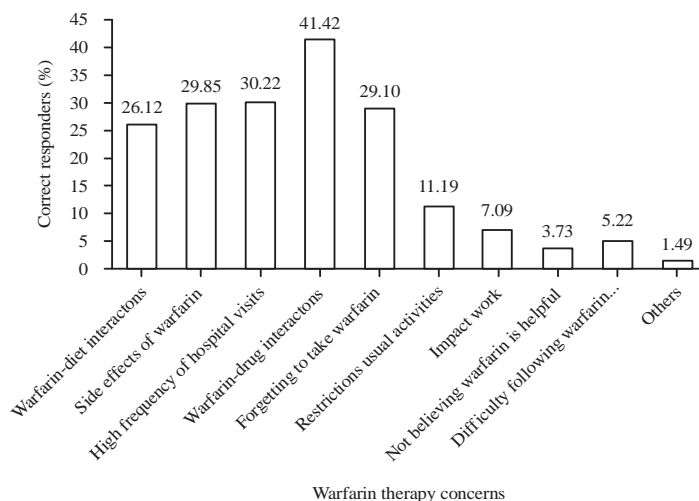


Fig. 3: Percent distribution of warfarin therapy concerns among the respondents

Table 2: Issues on patients' knowledge of warfarin treatment (n = 268)

Items	Correct responses (n)	Percentage
Warfarin's adverse effects		
Symptoms of bleeding	201	75.00
Frequency of monitoring signs of bleeding	150	55.97
Association between warfarin dosage, INR control and subsequent clinical complication	135	50.37
Impact of warfarin on intramuscular injections	92	34.33
Warfarin administration		
Color and number of daily warfarin tablets prescribed	208	77.61
Actions to take if a warfarin dose is missed	185	69.03
Target INR range	175	65.30
Warfarin drug interactions		
Consulting doctors when starting a new medicine	220	82.09
Medicines that interact with warfarin	130	48.51
Warfarin diet interactions		
Importance of keeping a consistent diet	196	73.13
Food that interacts with warfarin	140	52.24

Patient knowledge was analyzed using independent samples t-test and Mann Whitney U test as appropriate

Table 3: Distribution of responses to each statement in the satisfaction scale (n = 268)

Statements	Strongly agree		Agree		Neutral		Disagree		Strongly disagree	
	No.	%	No.	%	No.	%	No.	%	No.	%
Care provider at the warfarin clinic can give you useful and sufficient instructions on your treatment	91	33.96	160	59.70	7	2.61	6	2.24	4	1.49
You have been given enough time to discuss therapy with the staff your visits	88	32.84	162	60.45	11	4.10	5	1.87	2	0.75
Staff at the clinic are friendly	125	46.64	132	49.25	7	2.61	2	0.75	2	0.75
Since you began your treatment at this hospital, you have felt reassured about your warfarin treatment	77	28.73	161	60.07	20	7.46	10	3.73	0	0.00
Since you began your treatment at this clinic, your blood INR results have been better controlled	68	25.37	147	54.85	41	15.30	11	4.10	1	0.37
You are satisfied with the frequency of your appointments at this hospital for your warfarin follow ups	65	24.25	144	53.73	42	15.67	16	5.97	1	0.37
You are satisfied with your waiting time in the warfarin clinic to see the care provider	35	13.06	100	37.31	78	29.10	45	16.79	10	3.73

Patient satisfaction was analyzed using independent samples t-test and Mann Whitney U test as appropriate

better outcome. It is understood that older patients are usually come with polypharmacy as a result of their multiple chronic

conditions. Patients' health might be at risk on top of lacking better INR control¹⁴.

As shown in our findings, patients' satisfaction with provided service was not optimal but rather moderate. The main concern was the extended waiting time to see the healthcare provider at the clinic. As it is the case worldwide, lack of trained healthcare workers leads to less patient access to intended care¹⁵. In this study particularly, more trained staff were recruited to overcome this concern. Pharmacists are proven to administer an outstanding patient care in multidiscipline settings. Increasing number of staff in anticoagulation clinics will eventually improve patient communication leading to better INR control.

Surveyed patients demonstrated their worries about possible drug interaction with other drugs or diet. Worries also shown regarding adverse drug events. Concerns were valid and could be alleviated with better educational programs and improved patient-clinic communication. Drug use adherence (compliance) with prescriptions and clinic instructions will reduce possible adverse events as a result of various interactions or missed doses. Several patients might afford and could be willing to use home warfarin testing which will provide assurance to INR levels in addition to reducing clinic visits that was of another concern to few patients¹⁵. When providing optimal education and required training to warfarin patient, some patient might be able to self-monitor their therapy. This was also introduced in previous studies assuring more INR control, less clinic visits and improved patient safety^{16,17}. Home INR monitoring might be a stimulus for tighter control, less off therapeutic range values and happier patients.

The ultimate goal of keeping patient within desired therapeutic range is to prevent associated risk for off-range values. INR levels are results of human body reaction to warfarin intake which is affected by many environmental or genetic factors. Patient diet and eating habits are easily manageable with directed educational programs that will eventually produce a better INR control. On the other hand, genetic factors (presence of genetic sequence variants, VKORC1 or CYP2C9), may lead to patient overreaction to regular doses of warfarin (average dose). In such cases, usual anticoagulation clinic follow-ups may not produce anticipated results^{18,19}. Patient reaction to warfarin due to genetic differences cannot be manipulated.

Better INR control was noted more in patients' categories with better knowledge, higher satisfaction and less warfarin use concerns. As mentioned earlier clinic conducted programs are able to positively affect these categories producing desirable INR values.

CONCLUSION

This study findings trending toward more emphasis on patient directed educational programs in anticoagulation clinics. There is a vast shortage in patients' knowledge and satisfaction with warfarin therapy. Such deficits lifted the threshold of concerns with warfarin use and negatively affected INR control. Drug therapy adherence correlated negatively with less knowledge, level of education and satisfaction with provided services. All of which had produced less INR control.

In order to obtain desired INR levels in any anticoagulation clinic, one should consider all the discussed factors, establish a well-designed patient oriented educational program for warfarin users focusing on improving drug use knowledge, alleviating therapy concerns, not to disregard continuous evaluation of anticoagulation clinic operation, introducing more trained staff and soliciting patients' opinions on every visit.

SIGNIFICANCE STATEMENTS

This study discovered the Saudi patients' anticoagulant knowledge, satisfaction and concern regarding warfarin therapy that can be beneficial with the threshold of concerns with warfarin use and subsequently affected INR control. This study help the researchers to uncover the critical areas of patient education regarding warfarin therapy that many researchers were not able to explore and this research open the way for completion of this project regarding genetic polymorphism affecting warfarin therapy.

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REFERENCES

1. Ansell, J., J. Hirsh, L. Poller, H. Bussey, A. Jacobson and E. Hylek, 2004. The pharmacology and management of the vitamin K antagonists: The seventh ACCP conference on antithrombotic and thrombolytic therapy. *Chest*, 126: 204S-233S.

2. Hylek, E.M., A.S. Go, Y. Chang, N.G. Jensvold, L.E. Henault, J.V. Selby and D.E. Singer, 2003. Effect of intensity of oral anticoagulation on stroke severity and mortality in atrial fibrillation. *N. Engl. J. Med.*, 349: 1019-1026.
3. Levine, M.N., G. Raskob, R.J. Beyth, C. Kearon and S. Schulman, 2004. Hemorrhagic complications of anticoagulant treatment: The seventh ACCP conference on antithrombotic and thrombolytic therapy. *Chest*, 126: 287S-310S.
4. Merli, G.J. and G. Tzanis, 2009. Warfarin: What are the clinical implications of an out-of-range-therapeutic international normalized ratio? *J. Thromb. Thrombolysis*, 27: 293-299.
5. Krynetskiy, E. and P. McDonnell, 2007. Building individualized medicine: Prevention of adverse reactions to warfarin therapy. *J. Pharmacol. Exp. Ther.*, 322: 427-434.
6. Wang, Y., M.C. Kong and Y. Ko, 2013. Comparison of three medication adherence measures in patients taking warfarin. *J. Thromb. Thrombolysis*, 36: 416-421.
7. Tang, E.O.Y.L., C.S.M. Lai, K.K.C. Lee, R.S.M. Wong, G. Cheng and T.Y.K. Chan, 2003. Relationship between patients' warfarin knowledge and anticoagulation control. *Ann. Pharmacother.*, 37: 34-39.
8. Sturgess, I.K., C.M. Hughes and J.C. McElnay, 2000. (P16) Refill compliance rates evidence for use as an outcome measure in practice-based research. *Pharm. J.*, 265: R35-R35.
9. Hess, L.M., M.A. Raebel, D.A. Conner and D.C. Malone, 2006. Measurement of adherence in pharmacy administrative databases: A proposal for standard definitions and preferred measures. *Ann. Pharmacother.*, 40: 1280-1288.
10. Smith, M.B., N. Christensen, S. Wang, J. Strohecker and J.D. Day *et al.*, 2010. Warfarin knowledge in patients with atrial fibrillation: Implications for safety, efficacy and education strategies. *Cardiology*, 116: 61-69.
11. Wang, Y., M.C. Kong, L.H. Lee, H.J. Ng and Y. Ko, 2014. Knowledge, satisfaction and concerns regarding warfarin therapy and their association with warfarin adherence and anticoagulation control. *Thrombosis Res.*, 133: 550-554.
12. Davis, N.J., H.H. Billett, H.W. Cohen and J.H. Arnsten, 2005. Impact of adherence, knowledge and quality of life on anticoagulation control. *Ann. Pharmacother.*, 39: 632-636.
13. Kurnik, D., R. Loebstein, H. Rabinovitz, N. Austerweil, H. Halkin and S. Almog, 2004. Over-the-counter vitamin K₁-containing multivitamin supplements disrupt warfarin anticoagulation in vitamin K₁-depleted patients A prospective, controlled trial. *Thromb. Haemostasis*, 92: 1018-1024.
14. Juurlink, D.N., 2007. Drug interactions with warfarin: What clinicians need to know. *CMAJ*, 177: 369-371.
15. Voller, H., C. Dovifat, J. Glatz, H. Kortke, U. Taborski and K. Wegscheider, 2004. Self management of oral anticoagulation with the IN Ratio system: Impact of a structured teaching program on patient's knowledge of medical background and procedures. *Eur. J. Cardiovasc. Prev. Rehab.*, 11: 442-447.
16. Morsdorf, S., W. Erdlenbruch, U. Taborski, J.F. Schenk and K. Erdlenbruch *et al.*, 1999. Training of patients for self-management of oral anticoagulant therapy: Standards, patient suitability and clinical aspects. *Semin. Thromb. Hemost.*, 25: 109-115.
17. Kulinna, W., D. Ney, T. Wenzel, D.L. Heene and J. Harenberg, 1999. The effect of self-monitoring the INR on quality of anticoagulation and quality of life. *Semin. Thromb. Hemost.*, 25: 123-126.
18. Aquilante, C.L., T.Y. Langae, L.M. Lopez, H.N. Yarandi and J.S. Tromberg *et al.*, 2006. Influence of coagulation factor, vitamin K epoxide reductase complex subunit 1 and cytochrome P450 2C9 gene polymorphisms on warfarin dose requirements. *Clin. Pharmacol. Ther.*, 79: 291-302.
19. Sconce, E.A., T.I. Khan, H.A. Wynne, P. Avery and L. Monkhouse *et al.*, 2005. The impact of *CYP2C9* and *VKORC1* genetic polymorphism and patient characteristics upon warfarin dose requirements: Proposal for a new dosing regimen. *Blood*, 106: 2329-2333.