



Validation of a Knowledge Test in Turkish Patients on Warfarin Therapy at an Ambulatory Anticoagulation Clinic

Ayaktan Antikoagülasyon Kliniğinde Varfarin Tedavisi Alan Türk Hastalarında Bir Bilgi Testinin Validasyonu

İ Meltem TÜRKER¹, İ Mesut SANCAR¹, İ Refik DEMİRTUNÇ², İ Nazlıcan UÇAR¹, İ Osman UZMAN³, İ Pınar AY⁴, İ Ömer KOZAN⁵, İ Betül OKUYAN^{1*}

¹Marmara University Faculty of Pharmacy, Department of Clinical Pharmacy, Istanbul, Turkey

²University of Health Sciences Turkey, Haydarpaşa Numune Training and Research Hospital, Clinic of Internal Medicine, Istanbul, Turkey

³Kars Sarıkamış State Hospital, Clinic of Cardiology, Kars, Turkey

⁴Marmara University Faculty of Medicine, Department of Public Health, Istanbul, Turkey

⁵Baskent University, Istanbul Hospital, Clinic of Cardiology, Istanbul, Turkey

ABSTRACT

Objectives: This study aimed to evaluate the validity and reliability of an oral anticoagulation knowledge (OAK) test in Turkish patients on warfarin therapy at an anticoagulant outpatient clinic.

Materials and Methods: This study was conducted at an ambulatory anticoagulation clinic and included patients older than 18 years who had been using warfarin for at least six months. Patients' demographic and clinical data were collected. Internal consistency was calculated using the Kuder-Richardson 20 (KR-20) coefficient, and the test-retest reliability of the Turkish version of the OAK test was assessed.

Results: Patients' mean age was 59.83±11.93 (26-90) years (n=240; 133 women). The mean score of the OAK test was 14.19±3.01. The test-retest reliability of the scale (n=30) was moderate for the total score (p<0.001). The KR-20 value, a measure of internal consistency, was 0.671. Patients of a younger age and higher educational level were more likely to have higher levels of anticoagulation knowledge than patients of an older age and lower education level (p<0.05 for both comparisons).

Conclusion: The Turkish version of the OAK test can be used to determine the patients' knowledge on oral anticoagulation.

Key words: Warfarin, anticoagulant, knowledge, pharmacist

ÖZ

Amaç: Bu çalışmada, bir antikoagülan polikliniğinde varfarin tedavisi alan Türk hastalarda oral antikoagülasyon bilgisi (OAK) testinin geçerlilik ve güvenilirliğinin değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntemler: Bu çalışma ayaktan antikoagülasyon kliniğinde yürütülmüştür ve en az altı aydır varfarin kullanan 18 yaşından büyük hastaları kapsamaktadır. Hastaların demografik ve klinik verileri toplanmıştır. Kuder-Richardson 20 (KR-20) katsayısı kullanılarak iç tutarlılık hesaplanmış ve OAK testinin Türkçe versiyonunun test-tekrar test güvenilirliği değerlendirilmiştir.

Bulgular: İki yüz kırk hastanın (133 kadın) yaş ortalaması 59,83±11,93 (26-90) idi. Oral antikoagülasyon bilgi testinin ortalama skoru 14,19±3,01 olarak hesaplanmıştır. Ölçeğin test-tekrar test güvenilirliği (n=30) toplam skor için orta düzeyde bulunmuştur (p<0,001). İç tutarlılık güvenilirliği, hesaplanan KR-20 değeri (0,671) ile doğrulanmıştır. Daha genç ve yüksek eğitim düzeyindeki hastalar, daha ileri yaşta ve düşük eğitim düzeyindeki hastalarla karşılaştırıldığında daha yüksek antikoagülasyon bilgisine sahip olarak belirlenmiştir (her iki karşılaştırma için p<0,05).

Sonuç: Hastaların oral antikoagülasyon konusundaki bilgilerini belirlemek için OAK testinin Türkçe versiyonu kullanılabilir.

Anahtar kelimeler: Varfarin, antikoagülan, bilgi, eczacı

*Correspondence: betulokuyan@yahoo.com, Phone: +90 216 777 52 00 ORCID-ID: orcid.org/0000-0002-4023-2565

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INTRODUCTION

Warfarin is mostly used as an oral anticoagulant for the prophylaxis and management of primary and secondary thromboembolism.¹⁻³ Although, recently, new oral anticoagulants have been developed, warfarin remains the most commonly prescribed vitamin K antagonist in the clinical settings.²⁻⁴ However, patients are subject to risks when on warfarin.^{1,2} Bleeding is a common adverse event that occurs at an annual rate of 7-8% among patients on warfarin. Additionally, it was reported that the most common cause of drug-induced emergency department admissions was related to warfarin use.⁵ Warfarin's narrow therapeutic range and wide dose-response variability should be considered when managing its use in treatment.¹ Patients treated with warfarin should be closely monitored to ensure their adherence to warfarin therapy and detect and prevent adverse events.⁶ Serious problems may occur if patients adhered poorly to medications, especially those with a narrow therapeutic range, such as warfarin. Missed doses decrease the efficacy of the medication, and overdoses cause various adverse events.⁷

Wang et al.⁸ showed a relationship between the level of medication adherence and level of medication knowledge among patients using warfarin. In the study conducted in Turkey, poor medication adherence of patients receiving anticoagulant therapy was associated with a poor time in therapeutic range (TTR), poor warfarin knowledge, and higher bleeding score.⁹ Based on the findings of a multicenter study conducted in Turkey, poor knowledge of potential warfarin-food interactions was more common in older patients.¹⁰

To our best knowledge, there is no valid and reliable anticoagulation knowledge test in Turkish. Few validated anticoagulation knowledge tests exist for this purpose.¹¹⁻¹³ The oral anticoagulation knowledge (OAK) test used in our study was short compared with other questionnaires^{11,12} and is commonly used as a reliable and valid tool in the United States,¹⁴ Malaysia,¹⁵ and Brazil¹¹ to identify and evaluate patients' knowledge of anticoagulation. This study aimed to evaluate the validity and reliability of a knowledge test in Turkish patients on warfarin therapy at an ambulatory anticoagulation clinic.

MATERIALS AND METHODS

Participants and setting

A previous research suggested that the number of test items should be multiplied by 10 to obtain the number of participants, so, for this methodological study, 200 patients were required for an adequate sample size.¹⁶ On allowing for a 20% loss due to missing data or participants discontinuing the medication during the study, the necessary sample size was 240 patients.

This methodological study was conducted at the outpatient anticoagulation clinic of a university hospital located in Istanbul between 15 April 2017 and 15 October 2017. The clinic provided a service that adjusted the patients' warfarin dose according to their international normalized ratio (INR). Patients older than 18 years who had been using warfarin for at least the past six months and had at least four INR measures in their medical

records were eligible for this study. Patients who could not read were excluded from the study.

The study was approved by the Ethical Committee of Marmara University, Institute of Health Sciences (03.04.2017-121). Informed consent was obtained from all participants.

Data collection

Patients' demographic and clinical data, including their age, gender, educational level, total number of medications used, indication for oral anticoagulant therapy, and previous INR measurements, were collected using individual interviews and patients' medical charts. Individual interviews were conducted by a single researcher (MT). At least four consecutive INR measurements taken at least a month and no more than two months apart were retrospectively recorded from patients' medical charts. Patients' TTR was calculated using the method developed by Rosendaal et al.¹⁷

Translation and cross-cultural adaptation of the OAK test

Permission to use the OAK test for this study was obtained from Zeolla et al.¹⁴ This knowledge test includes a total of 20 questions about follow-up, drug-drug interactions, fundamental medication information, adverse effects, and nutritional problems. Higher test scores indicate a better level of oral anticoagulant knowledge.¹⁴ Patients were classified into three groups according to their total score in the OAK test based on previous studies.^{13,18} Patients with total OAK test scores of less than 10 (<50%) had low anticoagulation knowledge; patients with total OAK test scores between 10 and 15 (50-75%) had moderate anticoagulation knowledge; patients with total OAK test scores of more than 15 (>75%) had good anticoagulation knowledge.

The original English test was translated into Turkish independently by two native Turkish speakers, who were also fluent in English. Then, two researchers (MS and RD) reviewed the translations and reconciled them into one Turkish version. This Turkish version was back translated into English independently by two native English speakers, who were also fluent in Turkish. Differences between this draft English version and the original English version were evaluated by two researchers (MT and BO). After the translation process, the draft Turkish version was evaluated for grammar, conceptual equivalence, and cultural compatibility by a group of experts (two clinical pharmacists, an internal medicine specialist, a cardiologist, a nurse, and a Turkish literature lecturer). A pilot study was conducted on a group of patients (n=20) for cultural adaptation. It took approximately 10-12 minutes to complete the test. To assess the test-retest reliability, the knowledge test was completed by 30 patients from the study population within two weeks. To analyze the construct validity, demographic and clinical data in each group were evaluated.

Statistical analysis

Categorical data were presented as numbers and percentages. Continuous data were presented as mean \pm standard deviation or median and interquartile range (IQR). The Kolmogorov-Smirnov test was used for the normality of distribution. The test-retest

reliability was assessed using Spearman's correlation test. To measure the internal consistency, a Kuder-Richardson 20 (KR-20) coefficient value was calculated for the OAK test. Continuous data between two or more groups were analyzed using the Mann-Whitney U test or Kruskal-Wallis test, respectively. Categorical data were analyzed using the chi-square test. In this study, p values <0.05 were statistically significant.

RESULTS

This study included 240 patients (133 women) who were on warfarin. Patients' demographic and clinical data are shown in Table 1. Participants' mean age was 59.83 ± 11.93 (26-90) years. The mean score of OAK test was 14.19 ± 3.01 . The most frequent wrong responses were related to drug-drug and drug-food interactions. Less than half of the patients did not know the correct way to distinguish between different strengths of warfarin. The correct answer to this question varied from that in the original scale developed by Zeolla et al.¹⁴, due to differences between the national health systems in each country. This was emphasized in the validation study of the Brazilian version of the OAK test.¹ The right answer in Turkish version was "size" rather than "color", and this was taken into consideration during scoring. The percentage of correct answers, corrected item-total correlation, and KR-20 coefficients, if each item was deleted, is shown in Table 2.

The KR-20 coefficient was 0.671. There was a strong correlation between the test-retest results of patients' total score in the OAK test at baseline and two weeks later ($r=0.739$; $p<0.001$; data not shown).

Patients of a younger age and higher educational level were more likely to have higher OAK test scores than those of an older age and lower educational level ($p<0.05$; Table 3). There was no significant difference in TTR scores or the number of medications used between patients with low, moderate, and high anticoagulant knowledge ($p>0.05$; Table 3). Evaluation of related factors (demographic and clinical characteristics of the patients) in groups according to patients' anticoagulant knowledge is shown in Table 3.

DISCUSSION

In this study, the validity and reliability of the Turkish version of the OAK test were evaluated. The Turkish version of the OAK test was valid and reliable. The KR-20 value in the study conducted in Brazil was 0.818.¹ In the United States, the KR-20 value was 0.76.¹⁴ Although the value obtained in our study was acceptable, it was lower than the values obtained in the previously mentioned studies. The rate of the right responses in the present study was similar to that obtained by da Silva Praxedes et al.¹ The total number of correct responses in studies conducted in the United States,¹⁴ Brazil,¹ India,¹⁸ and Saudi Arabia¹³ was also similar to our study.

According to a study conducted in India, 50% of patients using oral anticoagulants had OAK test of less than 10, 37% had scores between 10 and 15, and 13% had scores greater than 15.¹⁸ According to a study conducted in Denmark, patients

Table 1. Demographic and clinical characteristics of the participants (n=240)

Characteristics	
Age, mean (SD)	59.83 (11.93)
Median (IQR)	61.0 (52.0-68.8)
Age group, n (%)	
18-40	16 (6.7)
41-60	102 (42.5)
61-80	116 (48.3)
>80	6 (2.5)
Sex, n (%)	
Female	133 (55.4)
Male	107 (44.6)
Marital status, n (%)	
Married	199 (82.9)
Single	41 (17.1)
Education, years, mean (SD)	6.6 (3.7)
Median (IQR)	5.0 (5.0-8.0)
Education group according to the years of education, n (%)	
<8 years	164 (68.3)
≥8 years	76 (31.7)
TTR, mean (SD)	52.2 (30.4)
Median (IQR)	52.0 (28.0-77.0)
Group of TTR, n (%)	
TTR <50%	114 (47.5)
TTR 50-75%	64 (26.7)
TTR >75%	62 (25.8)
The number of medications used, mean (SD)	3.68 (2.37)
Median (IQR)	3.0 (2.0-5.0)
Polypharmacy (defined as the concurrent use of 5 or more medications), n (%)	
Yes	174 (72.5)
No	66 (27.5)
Indication, n (%)	
Prosthetic heart valve	126 (46.5)
AF	62 (22.9)
Valvular heart disease	35 (12.9)
DVT/PTE	44 (16.3)
Acute MI/recurrent TIA	5 (1.5)
20 questions of oral anticoagulation knowledge test percentage mean ± SD	
Median (IQR)	14.2±3.0 12.0 (14.0-16.0)
Oral anticoagulation knowledge categories, n (%)	
<50% (low level of knowledge)	21 (8.8)
50-75% (moderate level of knowledge)	134 (55.8)
>75% (high level of knowledge)	85 (35.4)

SD: Standard deviation, TTR: Time in therapeutic range, AF: Atrial fibrillation, DVT: Deep vein thrombosis, PTE: Pulmonary thromboembolism, MI: Myocardial infarction, TIA: Transient ischemic attack

Table 2. Percentage of correct answers, corrected item-total correlation, and Kuder-Richardson coefficients if an item is deleted (n=240)

Questions	Correct answers	Percentage of correct answers (n)	Corrected item-total correlation	Kuder-Richardson coefficients if an item is deleted
1. Missing one dose of warfarin:	b. Can alter the drug's effectiveness	66.7 (160)	0.293	0.654
2. You can distinguish between different strengths of warfarin tablets by what?	c. Size	36.2 (87)	0.205	0.665
3. A patient on warfarin therapy should contact the physician or healthcare provider who monitors it when:	d. All of the above	85.0 (204)	0.189	0.665
4. Occasionally eating a large amount of leafy greens vegetables while taking warfarin can:	b. Reduce the effectiveness of the warfarin	41.7 (100)	0.295	0.654
5. Which of the following vitamins interacts with warfarin?	d. Vitamin K	40.8 (98)	0.438	0.635
6. When is it safe to take a medication that interacts with warfarin?	b. If your healthcare provide is aware of the interaction and checks your PT/INR ("Protime") regularly	60.8 (146)	0.214	0.664
7. PT/INR ("prothrombin time") test:	a. A blood test used to monitor your warfarin therapy	98.3 (236)	0.063	0.672
8. Warfarin may be used to:	a. Treat people that already have a blood clot	99.2 (238)	0.129	0.670
9. A patient with a PT/INR ("Protime") value below their "goal range":	b. Is at an increase the risk of having a clot	77.9 (187)	0.365	0.646
10. Taking a medication containing aspirin or other non-steroidal antiinflammatory medications such as ibuprofen while on warfarin will:	b. Increase your risk of bleeding from the warfarin	60.0 (144)	0.339	0.648
11. A person on warfarin should seek immediate medical attention:	b. If they notice blood in their stool when going to the bathroom	48.3 (116)	0.292	0.654
12. Skipping even one dose of your warfarin can:	c. Cause your PT/INR ("Protime") to be below the "goal range"	79.2 (190)	0.261	0.658
13. Drinking alcohol while taking warfarin:	b. May affect your PT/INR ("Protime")	82.1 (197)	0.367	0.647
14. Approximately how often should you have PT/INR ("prothrombin time") measured when you are stabilized with the correct warfarin dose (PT/INR is at target values)?	b. Once a month	94.2 (226)	0.251	0.662
15. It is important for a patient taking warfarin to monitor for signs of bleeding:	b. At all times	80.8 (194)	0.038	0.681
16. The best thing to do if you miss a dose of warfarin is to.....?	b. Take the next scheduled dose and tell your healthcare provider	81.2 (195)	0.169	0.668
17. When it comes to diet, people taking warfarin should:	c. Be consistent and eat a diet that includes all types of food	84.2 (202)	0.086	0.675
18. Each time you get your PT/INR ("Protime") checked, you should:	d. Let your doctor know if you missed any doses of warfarin	90.0 (216)	0.108	0.671
19. Which of the following over-the-counter products is most likely to interact with warfarin?	b. Herbal/dietary supplements	32.9 (79)	0.421	0.638
20. A patient with a PT/INR ("Protime") value above the "goal range":	c. Is at an increased risk of bleeding	79.6 (191)	0.313	0.652

PT: Prothrombin time, INR: International normalized ratio

Table 3. Factors (demographic and clinical characteristics of the patients) in groups divided according to patients' anticoagulation knowledge test score (n=240)

	The anticoagulation knowledge test score			P
	<50% (n=21)	50-75% (n=134)	>75% (n=85)	
Age, mean \pm SD	64.4 \pm 13.0	61.2 \pm 11.3	56.4 \pm 11.9	<0.01
Median (IQR)	68.0 (53.5-72.5)	61.0 (53.8-69.2)	58.0 (48.0-64.0)	
Education, years, mean \pm SD	6.5 \pm 4.0	5.4 \pm 2.9	8.5 \pm 3.9	<0.001
Median (IQR)	5.0 (5.0-9.5)	5.0 (5.0-5.0)	8.0 (5.0-11.0)	
TTR, mean \pm SD	49.5 \pm 27.0	51.4 \pm 30.8	54.0 \pm 30.8	NS
Median (IQR)	45.0 (29.0-74.5)	50.5 (28.0-76.0)	59.0 (26.0-80.5)	
The number of medications used, mean \pm SD	3.6 \pm 2.4	3.7 \pm 2.4	3.7 \pm 2.3	NS
Median (IQR)	3.0 (2.0-5.0)	3.0 (2.0-5.0)	3.0 (2.0-5.0)	
Gender				
Female, n (%)	5 (2.1)	81 (33.8)	47 (19.6)	<0.01
Male, n (%)	16 (6.7)	53 (22.1)	38 (15.8)	
Education group according to the years of education				
<8 years, n (%)	15 (6.2)	108 (45.0)	41 (17.1)	<0.01
\geq 8 years, n (%)	6 (2.5)	26 (10.8)	44 (18.3)	
Marital status				
Married, n (%)	19 (7.9)	107 (44.6)	73 (30.4)	NS
Single, n (%)	2 (0.8)	27 (11.2)	12 (5.0)	

SD: Standard deviation, TTR: Time in therapeutic range, NS: Non-significant

had a low knowledge of vitamin K antagonist.¹⁹ In a study conducted in Toronto, more than half of the participants had insufficient knowledge of vitamin K antagonists.²⁰ Patients had higher knowledge levels in our study compared with these previous studies. In a study conducted in Brazil, similar to the one conducted in Turkey, 71% had insufficient knowledge.¹ In a study conducted in Malaysia, 11.2% had insufficient knowledge.¹⁵ When the OAK test score in a study conducted in Singapore was evaluated, patients had a moderate knowledge level.⁸ However, another study reported that more than half of the participants had a poor knowledge level.¹³ Consistent with this study, other studies reported similar results, ranging from 61.2% to 70%.^{21,22} These results highlight the need for intensive training and awareness programs to increase patients' knowledge of such serious issues.

In this study, women had better knowledge of oral anticoagulants than men. Similar results were obtained in a study conducted in Saudi Arabia.^{13,21} In other studies, contrasting results were obtained.^{20,22,23} Studies conducted in Toronto²⁰ and in North India² indicated that the total OAK test score was higher when participants had a higher educational level. These results were similar to our findings and those from other studies, which showed that OAK test scores were lower in older patients.^{2,14,24,25}

In this study, no significant correlation was found between TTR and OAK test scores, which suggested that there was no

correlation between good anticoagulant knowledge and good INR control. A similar result was obtained in studies conducted in Saudi Arabia.^{13,23} Similar to our study, using the Rosendaal method, some international studies concluded that there was no significant relationship between patients' knowledge of oral anticoagulants and anticoagulation controls.^{15,26,27} In another study conducted in the United States, it was concluded that there was no significant correlation between patients' knowledge of warfarin and their INR control.²⁸ In a study conducted in China, a different result was obtained.²⁹ Shilbayeh et al.¹³ stated that incompatible results could be attributed to differences in test items, languages, settings, INR control measures, and different sample sizes.

When examining the OAK tests developed so far, the scale we used in terms of both content and validity was like the scale developed by Briggs et al.¹¹ However, while the scale we used was valid only for vitamin K antagonists, the scale developed by Obamiro et al.¹² can be used for vitamin K antagonists and direct-acting oral anticoagulants. While the scale, which is developed by Obamiro et al.¹² includes multiple-choice and open-ended questions, the scale we used included only multiple-choice questions. Based on our best knowledge, no existing validated tests assess patients' knowledge of oral anticoagulants in our country.

In future studies, the potential impact of duration of warfarin therapy on patients' anticoagulant knowledge test result should be evaluated. Besides assessing the patients' anticoagulant knowledge level, the problems related with medication

administration (such as dose adjustment difficulty, which is, particularly, due to limited strengths of warfarin tablets in Turkey) might be also assessed. It is necessary to provide comprehensive patient education for patients' receiving warfarin therapy. Using the OAK test in a clinical setting could provide an opportunity for healthcare providers to identify and resolve patients' misunderstandings and/or correct any misinformation they may have encountered. This brief test could easily be conducted in outpatient clinics, as it only requires a short time to complete (10-12 minutes).

Study limitations

The generalizability of the results to different patient groups in Turkey may be limited in this study, because it was conducted in a single outpatient clinic in Turkey. Another limitation of the study was that the OAK test designed by Zeolla et al.¹⁴ was to be self-administered by individuals with an educational level of at least the seventh grade. However, in most studies, including this study, which used the OAK test, individuals with an educational level lower than the seventh grade took the test.

CONCLUSION

The Turkish version of OAK test can be used to determine the patients' knowledge of oral anticoagulation. This test would be helpful for identifying patients who need education and counseling regarding warfarin therapy. Additionally, it can be used to assess changes in patients' knowledge after receiving education and/or counseling. The test can be used to identify and resolve patients' misunderstandings of anticoagulant therapy and/or correct misinformation to which they may have been exposed. Test items may remind patients and providers of key points to consider during warfarin therapy.

Conflict of interest: No conflict of interest was declared by the authors. The authors are solely responsible for the content and writing of this paper.

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