Survey of Knowledge and Attitude of Pharmacists about Direct Oral Anticoagulants: A Cross-Sectional Study

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ABSTRACT

Background: Direct oral anticoagulants (DOACs) are increasingly used due to fewer side effects, predictable pharmacokinetics, lower potential for drug interactions. Different levels of awareness among health care professionals have been reported.

Methods: The main objectives of this study were to investigate the knowledge and attitude of pharmacists about direct oral anticoagulants. The present study was a descriptive cross-sectional study performed in Kermanshah province, Iran. The validated researcher-made questionnaire included questions about demographic characteristics and specialized questions that assessed the knowledge and attitude of pharmacists towards new oral anticoagulants.

Results: Out of 126 pharmacists participating in this study, 67 (53.2%) were male. The mean scores of knowledges and attitude in pharmacists were 64.94±5.84 and 28.62±3.98, respectively. The most common oral anticoagulant with a direct effect dispensed by pharmacists was rivaroxaban (77.4%). There was also a significant relationship between pharmacists' attitudes and their place of activity (P = 0.024).

Conclusion: The results of this study showed that pharmacists had an acceptable knowledge and low attitude about DOACs.

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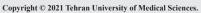

Introduction

Deep vein thrombosis is a major preventable cause of mortality and morbidity throughout the world. After heart attacks and strokes, deep vein thrombosis is the third cause of vascular death (1). In addition, the Atrial Fibrillation (AF), as the most common cardiac arrhythmia, is associated with a twofold increase in the risk of heart stroke (2). In the EU, it is estimated that the number of patients with the AF who are older than 55 will increase by more than twice by 2060 [8.8 vs. 17.9 million patients in 2010 and 2060, respectively] (3). While, for years, vitamin K antagonists, especially warfarin, were the mainstay of the anticoagulant therapy for the AF, the direct anticoagulants (DOACs) (rivaroxaban, dabigatran, apixaban, and edoxaban) are recently recommended instead of warfarin for atrial fibrillation and deep vein thrombosis for most patients (4). The Direct Oral Anticoagulants (DOACS) were introduced in 2010 and are still a relatively new class of oral anticoagulants. Dabigatran, as a direct thrombin inhibitor, was the first DOAC introduced, followed by coagulation factor Xa inhibitors (rivaroxaban, apixaban, edoxaban) (5). Rapid function, more predictable pharmacokinetics, fixed-

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dose regimens, lower potential for drug-drug and food-drug interactions, and less monitoring have made the DOACs an attractive treatment option for both health care providers and patients (6).

However, the direct oral anticoagulants are not without limitations. Relative short half-life, increase in gastrointestinal bleeding (especially dabigatran and rivaroxaban), requiring dose adjustment in renal and hepatic impairments and in elderly patients, and contraindication in pregnant and lactating women are among major limitations of the DOACs (5, 7). Although these agents are the more favorable options for thrombosis prophylaxis and treatment, different aspects of anticoagulant pharmacology, including the lack of standard monitoring, the unavailability of standard serum levels, the potential important interactions, and the wide availability of antidotes require health care providers' further vigilance in order to minimize the potential complications associated with these agents.

Traditionally, pharmacists were involved in anticoagulation clinics in some countries. Pharmacist-managed anticoagulation has been associated with better anticoagulation, lower bleeding, and lower thrombotic events (8). Pharmacists who have educations on oral anticoagulants may also increase patient's compliance, correct medication use, and lower use of concomitant medications with potential interactions (9). In addition, most of the available studies were conducted in hospital and in-patient settings and a few studies are available for community pharmacies (10, 11). Furthermore, pharmacists' knowledge and awareness were not similar across all the studies (12, 13).

The aim of this study was to evaluate the community pharmacists' knowledge and attitudes on the direct oral anticoagulants in Kermanshah province, Iran.

Methods

This research was a cross-sectional descriptive-analytical study, which was conducted during May-December, 2020, in Kermanshah province. The sample size of the study was determined based on the list of the registered pharmacists according to the Food and Drug Administration Agency of Kermanshah. The study protocol was approved by the ethics committee of Kermanshah University of Medical Sciences (ethics code: IR.KUMS.REC.1399.319). The participants were also assured that their information would not be disclosed.

The present study was originally designed to evaluate the knowledge of both physicians and pharmacists about the DOACs. Therefore, using the previous study (5), the minimum sample size with $\alpha = 0.05$ was estimated to be 366 people. However, the total number of the registered physicians and pharmacists was determined according to the available list of 290 and 152 people, respectively. Finally, using a stratified sampling method, 240 physicians and 126 pharmacists were included in our study. In each

class, random sampling was performed by the use of random sampling numbers. In the present manuscript, only the data about the pharmacists is presented.

$$P=0.61 \quad z1\text{-}\alpha/2=1.96 \quad n=\frac{z^2_{(1-\frac{\alpha}{2})}\,P(1-P)}{d^2}=366$$

In this study, a researcher-made questionnaire including two domains of the pharmacists' knowledge and attitudes on the DOACs was prepared by the researcher according to the available guidelines (14). This questionnaire included the demographic information of the participants and 25 questions (supplement) related to the pharmacists' knowledge and attitude on DOACs. In summary, a paper-based questionnaire containing questions regarding the DOACs-related information as well as the mechanism of action, indications in different situations, side effects, doses in different populations, interactions, use in pregnancy and lactation, and antidotes was included in the. In addition, two open-ended questions about the pharmacists' practices and consulting during dispensing the DOACs as well as about participating as an audience regularly in continuous medical educations such as journal clubs or webinars were included at the end of the questionnaire (supplements 1, 2). To assess the validity, the structure and format of the questionnaire were checked by 10 pharmacists who had positions as faculty members, and the modifications were made. A revised questionnaire was given to 10 pharmacists with different experiences and work places. The calculated Cronbach's alpha was 0.74. The questionnaire was delivered to all the participants in a copy format by investigator (Z, V) to be filled in the right time.

The main outcomes of the study were the information obtained by evaluating the pharmacists' knowledge and attitudes about the DOACs.

The pharmacists' awareness and attitudes were reported to be 0-85 and 0-40, respectively.

The Kolmogorov-Smirnov test was used to examine the variables of the normal distribution. T-test was used to investigate the relationship between "the two-state variables" (gender, Journal Club, and academic degree) and "knowledge and attitude". The Spearman correlation coefficient was used to investigate the relationship between "age and work experience" and "knowledge and attitude". The one-way ANOVA was used to examine the relationship between "the activity variables" and "knowledge and attitude". All the statistical analyses were performed with SPSS (using the Statistical Package for Social Sciences version 16). The statistical significance level was considered to be 0.05.

Results

Out of the 126 pharmacists participating in the study, 67 (53.2%) were male. Most of the participants had PharmD

(93.7%) degree. Only 32.8% of the pharmacists participated in the Journal Club. Most the pharmacists (60.3%) had worked in community pharmacies. No clinical pharmacist was included in the study. The mean age of the pharmacists in the present study was 40.87 ± 7.82 years old. The pharmacists' average work experience was 10.43 ± 7.53 years, with a minimum and a maximum of 1 year and 40 years, respectively (Table 1).

Table 1. Demographic properties of the study participants.

Variables	Frequency
Age (years)	55.35±7.82
Sex	
Male	67
Female	59
Degree	
PharmD	118
PhD (non-clinical)	8
Journal club or Webinar participation	
Yes	41
No	84
Work place (n)	
Community pharmacist	76
Medication distribution company	31
Hospital and community	7
University and community pharmacy	6
University	3
Hospital	1
Experience (years)	10.53±7.43

The pharmacists' mean knowledge and awareness were 64.94 ± 5.84 and 28.62 ± 3.98, respectively. Frequency distributions of answers to the questionnaire for the questions about the pharmacists' knowledge (supplement 1) and attitudes (supplement 2) on the DOACs were presented. The most common oral anticoagulant dispensed by the pharmacists was rivaroxaban (77.4%), followed by warfarin (9.4%), and apixaban (3.8%), respectively. There was also a significant relationship between the pharmacists' attitudes and place of activity (P = 0.024). The correlations between the variables and the pharmacists' knowledge and attitudes are shown in Tables 2 and 3.

Table 2. Correlation between variables and knowledge of pharmacists.

Variables		Mean ± SD	P values
Sex	Male	65.19±6.34	0.63
	Female	64.66±5.25	
Academic degree	PharmD	64.99±5.67	0.73
	PhD	64.99±8.36	
Journal club	Yes	64.85±5.60	0.96
	No	64.99±8.36	
Work place	University faculty	60.0 ±7.0	0.57
	Community pharmacy	65.17±5.57	
	Hospital pharmacy	69.0 ±0.0	
	Company	64.68±6.62	
	Faculty and community	67.67±7.03	
	Community and hospital pharmacies	63.43±4.19	

Table 3. Correlations between variables and attitudes of pharmacists.

Variables		Mean ± SD	P values
Sex	Male	28.88±4.24	0.44
	Female	28.33±3.69	
Academic degree	PharmD	28.59±3.99	0.71
	PhD	29.12±4.18	
Journal club	Yes	28.63±3.86	0.96
	No	28.59±4.08	
Work place	University faculty	25.0±1.0	**0.024**
	Community pharmacy	28.19±4.02	
	Hospital pharmacy	35.0±0.0	
	Medication distribution company	39.09±3.62	
	Faculty and community	26.28±3.35	
	Community and hospital pharmacies	27.0±4.24	

As highlighted in Table 4, the community pharmacists had more focus on minor bleedings associated with the DOACs (41.5%), followed by the concurrent use of over-

the-counter medications or herbal medicines with potential drug interactions (15.09%), and the need for dental surgeries (13.20%), and had less emphasis on using higher doses of rivaroxaban with food to improve bioavailability.

Table 4. The practice of pharmacists.

Verbal Consults of community pharmacists	Frequency (%)
Minor bleeding	41.5
Over the counter and herbal medicine use consult	15.09
Dental procedure	13.20
Renal and liver dose dysfunctions	7.5
Pregnancy	7.5
Use of other antiplatelets	3.77
Use of higher doses with food	3.77

Discussion

In this study, the pharmacists' knowledge and attitudes on the direct oral anticoagulants were evaluated in Kermanshah province. The pharmacists had acceptable knowledge and low attitudes on the DOACs (64.94 ± 5.84% and 28.62 ± 3.98%, respectively). There was also a significant relationship between the pharmacists' attitudes and place of activity (P = 0.024). However, the correlations between their knowledge and experience, workplace, and participation in journal clubs were not significant.

Although several studies have evaluated pharmacists' knowledge and attitudes on warfarin (15, 16). Only a few ones have evaluated pharmacists' knowledge and awareness. Aiming to assess the pharmacists' potential to prescribe oral anticoagulants for atrial fibrillation, Sandhu et al. concluded that most pharmacists prefer to consult with a physician before prescribing the DOACs, and about 35% of the pharmacists were familiar with the DOACs and 25% were unsure of prescribing them (17). In addition, more than 20% of the responders considered the DOACs as risky medications.

Papastergiou et al., in a 2017 international survey with pharmacists found that there was a significant difference in the assurance of warfarin versus that of the DOACs (18). This study also showed that the pharmacists with clinical experiences had a better knowledge of the DOACs.

In a cross-sectional descriptive study in Qatar, El-Bardissy et al., evaluated the pharmacists' knowledge and attitude on the DOACs with a 26-question questionnaire (13). The questionnaire included 10, 11, and 5 questions about safety, efficacy, and the pharmacists' counseling domains, respectively (13). They found that the pharmacists had moderate awareness of the DOACs. The lowest awareness was observed for the efficacy domain and the highest for the counseling. However, in our study, mean awareness of 64.94 ± 5.84 was observed across all the participants, and a lower attitude was observed compared to the above study. In addition, similar to our study, the factors

including age and years of experience did not influence the pharmacists' awareness in El-Bardissy's study. They also showed that male-gender, the clinical, and the board-certified pharmacists had significantly higher awareness. In our study, no clinical pharmacist participated, almost all the participants had worked as community pharmacists, and no significant factors (e.g., academic, gender, place of work, participating in journal clubs) affected the pharmacists' awareness. The place of activity had a significant effect on the pharmacists' attitudes towards the drugs used in our study.

A KAP (Knowledge, Attitude, and Practice) study conducted by Hanafi et al., in Iran showed that most pharmacists have low knowledge and attitudes about a good pharmacy practice (19). The authors also showed that the pharmacists' experiences and increased education qualifications are predictors of a good pharmacy practice. Unfortunately, the curriculum of our pharmacy course includes more deductive contents rather than practical rotations. Therefore, the students' increased involvement in the inpatient care can increase the pharmacists' knowledge and attitudes on the DOACs.

In terms of practice, most of the pharmacists in our study focused on counselling on minor bleeding and use of over-the-counter and herbal medications, and a few pharmacists focused on using higher doses of rivaroxaban with food.

The main strength of our study was the use of an in-depth questionnaire that included the most comprehensive and practical information about the DOACs according to the most recent guidelines provided by the EU and the US. The major limitation of our study that can influence the results was a relatively small sample size that was calculated for only one area.

The findings of this study showed that the pharmacists had a relatively low to moderate knowledge about the DOACs. However, more educational courses are recommended to improve pharmacists' knowledge about the safety and efficacy of the direct oral anticoagulants. Finally, a larger sample size can define factors that influence the pharmacists' knowledge about the DOACs.

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