The first pharmacist-based warfarin-monitoring service in Iran

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Abstract

Objective A growing body of evidence indicates that pharmacist-based anticoagulation clinics can have equal and sometimes superior outcomes to those obtained through standard care. This paper assesses the adequacy of anticoagulation and the effect of consultation services in the first pharmacist-managed anticoagulation clinic in Iran.

Method The anticoagulation clinic of Masih Daneshvari Hospital was established by a clinical pharmacist. During a 14-month period all patients on warfarin therapy were referred to our clinic. Patients were monitored and consulted based on predetermined guidelines. The primary clinical outcome was the control of international normalized ratio (INR) within the therapeutic range. Data were gathered on the indication of warfarin therapy, the pharmacist's interventions, and the adverse drug effects experienced by the participants.

Key findings A total of 76 patients were included: 42.1% (age 50 ± 17 years, mean $\pm$ SD) were male. The primary indications for warfarin were treatment of deep-vein thrombosis or pulmonary emboli (46.1%) and mechanical valve replacement (23.7%). The main reason for referral of patients to clinic was routine monitoring (32.9%) and INR control (31.3%). The most common intervention by pharmacists was increasing the dose (31.6%). Of the referred patients 47.7% reached the target INR on follow-up visits, whereas 11.8% were not within the desired range. None of the clinical interventions performed by physicians for management of bleeding was compatible with guidelines. There was a trend between proper use of warfarin and reaching the target of INR control (odds ratio 2.97, $P = 0.09$).

Conclusion The results of this study demonstrate that a clinical-pharmacist-managed anticoagulation clinic offers not only safe and effective treatment but also is superior with respect to increased anticoagulation control.

Keywords anticoagulation clinic; clinical pharmacist; intervention; Iran; warfarin clinic

Introduction

Warfarin sodium is the most commonly prescribed oral anticoagulation drug worldwide for the treatment and prevention of various thromboembolic events. Because of its narrow therapeutic window successful anticoagulant use of this drug requires careful measurement and monitoring of the international normalized ratio (INR), ongoing patient education and effective communication between patients and their caregivers.[1–3] The management of therapy within this narrow window is complicated by numerous factors, including drug–drug and drug–food interactions, comorbidities and the variability of the patient's response to warfarin therapy.[4] Several studies have reported failure to reach the target INR, which may result in major complications.[5–7]

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There are different anticoagulation management services which vary by the type of staff who carry out anticoagulation monitoring, such as physician-based or pharmacist-based clinics.[2] Anticoagulation clinics are designed to coordinate and optimize the delivery of anticoagulant therapy by determining the appropriateness of therapy, managing warfarin dosing and providing continuous monitoring of the patient's INR value, dietary factors, concomitant medications and interfering disease state.[2,4]

A growing body of evidence indicates that anticoagulant clinics managed by clinical pharmacists have demonstrated improved care and sometimes are even less costly for patients receiving warfarin therapy compared to patients managed by their physician.[8–11]

Masih Daneshvari Hospital is a 250-bed, tertiary care, multidisciplinary teaching hospital in Tehran, Iran. About 10% of patients in our centre receive warfarin for different indications such as mechanical valve replacement or treatment of venous thromboembolic events. According to a report from the pharmacovigilance unit in the hospital, 4.67% of our patients experience some adverse events related to anticoagulation annually.[12] In Iran, physicians are in charge for warfarin monitoring and despite the importance of anticoagulation clinics no warfarin clinics officially exist.

This study was designed to assess the adequacy of anticoagulation, rates of anticoagulation-related events and the effect of consultation service and information resources for patients enrolled in the anticoagulation clinic before and after referral to our pharmacist-managed clinic.

Methods

The anticoagulation clinic was established in Masih Daneshvari Hospital in 2006 and it was headed by a clinical pharmacist (FF) from January 2006 to March 2007. Participants of this study were all patients on warfarin therapy who were referred to the clinic by a specialist physician during this period. The Ethics Committee of the hospital approved the study. There was no charge for the patients who were referred to this clinic. An evidence-based guideline was prepared, using the seventh American College of Chest Physician (ACCP) guidelines.[1] The guidelines were applied in monitoring patients, confirming the indication, assessing the duration of therapy, adjustment of dosages, performing interventions in cases of toxicity and arranging the schedule for follow-up visits. Therapeutic INR ranges for low-intensity (INR 2–3) and high-intensity (INR 2.5–3.5) indications were also adapted from the seventh ACCP guidelines.[1]

A patient was followed every 4 weeks if the target INR was obtained and maintained and every 8 weeks if the same warfarin regimen continued. All patients who had just initiated warfarin therapy would be returned to the anticoagulation clinic within 5 days. All patients for whom the warfarin dose had been changed had a mandatory follow-up visit and INR check within 7 days.

Considering dose, possible interactions, dietary factors and comorbidities, patients who could not sustain the therapeutic range were referred to their physician for further evaluation. Patient education included reasons for use and the benefits of warfarin therapy, bleeding and thrombosis symptoms,

interactions (drug, food, supplement and herbal) and missed-dose management. All studied patients received a standardized educational package that detailed the indication for therapy, the importance of complying with the regimen, the need for close monitoring, the potential risk of taking other medications, dietary considerations and the importance of self monitoring for evidence of bleeding or thromboembolic complications. Patients were also given a logbook to record their INR results.

The primary clinical outcome was achievement of therapeutic INR. The secondary outcomes were the clinical interventions for management of bleeding and patient education that all must be compatible with the seventh ACCP guidelines. Logistic regression analysis was performed to determine which of the variables were predictive of the target goal of INR. Patient satisfaction was determined using a patient satisfaction questionnaire, and was completed after the patient was consulted.

Results

During the study period, 76 patients receiving warfarin were referred to the anticoagulation clinic. Of these, 46 (60.2%) were inpatients. Patients had a mean age ($\pm$SD) of 50 ± 17 years, with a range of 16–76 years. Males comprised 42.1% of the cohort. Two major indications for warfarin use were deep-vein thrombosis or pulmonary emboli treatment (46.1%) and mechanical valve replacement (23.7%). The mean duration of warfarin therapy before the first clinic visit was 2157.65 ± 914.31 days. A total of 230 visits were made by 76 patients.

The main reason for patient referral was routine monitoring (32.9%) and INR control (30.3%) (Table 1). The most common intervention done by the pharmacist at the clinic was increasing the dose (31.6%). Other interventions are shown in Table 2.

Table 1 Main reasons for patient referral

Indication	Number (%)
Atrial fibrillation	1 (1.3)
Heart valve replacement	18 (23.7)
Left-ventricular dysfunction	3 (3.9)
Treatment of DVT or PE, first episode	35 (46.1)
Treatment of DVT or PE, recurrent	8 (10.5)
Prevention of DVT or PE	3 (3.9)
Other	8 (10.5)

Reasons	
Not indicated	1 (1.3)
Adverse drug reaction	1 (1.3)
Decreased INR	3 (3.9)
Dose adjustment for the first time	17 (22.4)
Increased INR	6 (7.9)
INR goal not reached	23 (30.3)
Routine monitoring	25 (32.9)

DVT, deep-vein thrombosis; INR, international normalized ratio; PE, pulmonary emboli.

Table 2 Pharmacist interventions

Interventions	Number (%)
Reduced dose	4 (5.3)
Hold dose	17 (22.4)
Increased dose	24 (31.6)
No change in dose	13 (17.1)
Modified dose due to interaction	4 (5.3)
Modified dose based on protocol	4 (5.3)
Repeat or check INR	4 (5.3)
Reschedule dosing for compliance enhancement	3 (3.9)
Scheduling a follow-up visit	1 (1.3)
Termination of warfarin therapy	2 (2.6)

INR, international normalized ratio.

Table 3 Warfarin adverse events observed during visits

Adverse events	Number (%)
Ecchymosis	1 (1.3)
Gastrointestinal bleeding	1 (1.3)
Minor bleeding	7 (9.2)
Purple toe syndrome	1 (1.3)
Thrombocytopenia	1 (1.3)
No adverse reaction	65 (85.5)

Of the referred patients, 47.4% reached the target INR on follow-up visits, whereas 11.8% were not within the desired range. None of the interventions (five patients) performed by physicians, including vitamin K or fresh frozen plasma (FFP) administration, was compatible with the seventh ACCP guidelines. In the mean follow-up of 14 months, 38.2% of patients received two or more medications, which could increase the effect of warfarin.

Table 3 shows adverse effects of warfarin usage during the clinic visits. No patient had a fatal event in the present study. A total of 672 interventions were documented by the pharmacist during all visits. Only 39 (52%) of patients could describe their own warfarin dosage schedule correctly and 37 (48.7%) had knowledge about the form of warfarin dosage and mechanism of action.

Logistic regression analysis showed a non-significant *P* value for the relationship between proper use of warfarin and reaching the target of INR in the therapeutic range (odds ratio 2.96, $P = 0.09$). There was no significant correlation between age, sex, comorbid diseases, drug interactions, duration of therapy or the patient's knowledge of maintaining INR within the therapeutic range.

Discussion

In the present study, 47.7% of patients reached the target INR on follow-up visits, a result that is compatible with data from other clinics in which up to 50% of patient INR values were within the target range.[8,13] However, about 27% of our patients did not attend a follow-up visit at the clinic.

About 12% of patients never reached the therapeutic INR range. This could be related to many factors such as referral to the clinic with no information about past medical history, false INR result due to laboratory errors and irregular follow-up because of old age or illiteracy.

The most common intervention (31.6%) was increasing the warfarin dose in order to reach the target INR value. It seems that physicians increase the dosage of warfarin very cautiously due to irregular monitoring and follow-up visits by the patients. Besides, our results show that, with even minor bleeding, physicians tend to aggressively reverse the effect of warfarin by over-administering vitamin K or FFP.

Our findings of adverse effects such as minor bleeding (9.2%) and major bleeding (1.3%) are consistent with those from other clinics that have reported 8 and 1.6%, respectively.[8]

One of the major objectives of such clinics is improving patient compliance through proper education and consultation, explaining the importance of drug monitoring and its interactions. Only 52% of our patients could describe their warfarin dosage schedule correctly. There was no significant relationship between our different variables and therapeutic INR, except for a trend between proper use of warfarin and the goal of maintaining INR within the therapeutic range. Although the correlation was not significant, the importance of regular monitoring, education and counseling of patients on warfarin therapy could not be rejected. Some 38.2% of our patients received two or more medications that increase the effect of warfarin. So, informing patients could have a great impact on outcomes and the prevention of possible side effects.

The anticoagulation clinic at the Masih Daneshvari Hospital is the first such clinic in Iran headed by a clinical pharmacist, although there are a few anticoagulation clinics that are established and run by physicians. No fee was charged to the patients who were referred to the clinic, unlike a respiratory clinic run by pulmonologists and which charges patients at least US$12 for the first 20 min of the visit.

Many studies have evaluated pharmacist-provided services for patients receiving warfarin[14–18] and indicated the benefit of pharmacists being in better control of anticoagulation, the reduced adverse effects such as bleeding and decreased hospital admissions and costs.[8,11,19,20] Other studies have compared pharmacist-based with physician-based anticoagulation clinics and showed that the pharmacists' performance is better than that of physicians in many aspects of warfarin monitoring.[15,19,21]

A trial conducted in Hong Kong compared a pharmacist-based with physician-based clinic: 137 patients were randomized to pharmacist- or physician-managed services. Both groups achieved high-quality anticoagulation control, and patients in the pharmacist-managed group spent more patient time (64%) in the therapeutic INR range than those in the physician-managed group (59%) ($P < 0.001$). However, the pharmacist-managed group had slightly but significantly better INR control and was less costly than the physician-managed group.[22]

About 90% of the patients had complete satisfaction from our services. One of the major objectives of such clinics is the improvement in patient compliance. Factors such as missed doses, lack of knowledge about the disease and treatment goals, experience of different side effects and the necessity for

a specific diet are important in patient compliance. A new method, especially in an overcrowded clinic, is the use of brochures, logbooks and booklets that inform patient about their disease and treatment and other related topics.[23] The warfarin patient education booklet was given and explained to all patients referred to our clinic.

Conclusion

This study has demonstrated the need for pharmacist-managed anticoagulation clinics which offer not only safe and effective treatment, but also may be superior with respect to increased anticoagulation control and may decrease the incidence of thromboembolic events. Currently ours is the only pharmacist-managed anticoagulation clinic in Iran, and the results of the present study may be used to establish the same model of care for anticoagulation management in other hospital settings in Iran.

Declarations

Conflict of interest

The Author(s) declare(s) that they have no conflicts of interest to disclose.

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