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An Audit Evaluating Anticoagulation Clinic Managed by Clinical Pharmacists in Jordan

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ABSTRACT

Background and Objectives : Warfarin is the most widely prescribed oral anticoagulant; it is highly effective for the treatment and prevention of venous and arterial thrombosis. The beneficial outcomes of warfarin therapy are dependent upon achieving and maintaining an optimal international normalized ratio (INR) therapeutic range. The aim of this study was to evaluate the impact of our newly established clinic at Queen Alia Heart Institute (QAHI) in the Royal Medical Services (RMS), Jordan.

Patients and Methods: An observational prospective study was carried out in a newly established anticoagulation clinic managed by two clinical pharmacists and one nutritionist in QAHI since September 2013 until June 2014. The patients (no= 250) who were on warfarin for at least two months referred to the clinic were included in our study. All patients or their care givers received a 45 minutes educational session and a warfarin booklet. Then they were followed up regularly for achieving and maintaining the target INR and developing any adverse events related either too high or low INR (>4.5 or <1.5, respectively).**Results:**The age range of this group of the patients who were referred to t he clinic was wide, 5-81 years. 65% of them were males, with the most common indications for Warfarin were aortic and mitral valves replacement, and atrial fibrillation.72% of the patients were not achieving therapeutic (T) INR 43% of them achieve the TINR within the first week, 28% within the second week, 17% within the third, 4% within the fourth and 8% exceeded 4 weeks. The proportion of time within TINR for all the patients during the whole period was 75%. Only 7% of the patients had low INR, <1.5 and 5% had high INR, >4.5 for one visit. No major thromboembolic or hemorrhagic events were reported.

Conclusion: The newly established clinic had achieved a considerable encouraging results and feedbacks in the short period of time since it had been established.

Keywords: Warfarin, international normalized ratio (INR), atrial fibrillation (AF), thrombosis, anticoagulation**.**

INTRODUCTION

Warfarin is the most widely prescribed oral anticoagulant; it is highly effective for the treatment and prevention of venous and arterial thrombosis. Warfarin use in clinical practice is extremely challenging because of narrow therapeutic range, its pharmacokinetics and pharmacodynamics is affected by genetic variables, drug interactions, comorbidities, patient age and diet, so individualized therapeutic approach is needed. As the majority of studies examining treatment setting in regards to the quality/safety of oral anticoagulation management, report that specialized anticoagulation clinic services are associated with better international normalized ratio (INR) control and reduced rates of hospitalizations/emergency visits due to adverse events related to anticoagulation, compared with standard community care (usual care/health maintenance Organization care).[1-5] Our institute identified the need to establish such clinics to improve warfarin management and provide safe and effective care for patients on warfarin.

The protocol was prepared in consensus between the managing clinical pharmacists and the referring physicians and approved by the Full term (RMS) higher medical committee.

The proposal included the goals of the clinic, the work flow of the clinic (referral form, patient initial visit, patient standard visit, and

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management of INR values if they are within, above or below therapeutic range) and scheduling preoperative management.

The goals and objectives for the anticoagulation clinic were to provide effective and safe anticoagulation therapy by achieving and maintaining therapeutic international normalized ratio (INR) quickly and safely; to improve the consistency of warfarin dosing, especially during weekends and statutory holidays; to improve patient outcomes and increase patient safety; to decrease errors in warfarin dosing; to ensure that patients' current and past medical history, medication history, and drug–food interactions were evaluated before a dose recommendation; and to decrease the frequency of INR testing.[6]

The aim of this prospective observational study was to evaluate the impact of our newly established clinic on patients' outcomes regarding time needed for achieving target INR, the proportion of time within therapeutic INR and finally controlling adverse events and preventing complications and hospitalization.

PATIENTS AND METHODS

The present study was conducted from September 2013 until June 2014 at Queen Alia Heart Institute (QAHI) anticoagulation clinic as a prospective observational study. The patients (no= 250) who were on warfarin for at least two months were included in our study. All patients or their caregivers received a 45 minutes educational session and a warfarin booklet; in the session the clinical pharmacist discussed with the patient or caregivers the indication of warfarin, mechanism of action, different dosage forms, target INR, INR monitoring, side effects, drug-warfarin interactions and duration for treatment. Then the nutritionist explained the food-warfarin interactions.

The patients were followed up regularly for achieving therapeutic (T) INR. Patients who were not achieving TINR the next visit were scheduled after one week. Patients who achieved TINR the next visit were scheduled after one month. For patients who were not achieving TINR we did dose adjustment according to **Baker *et al.*** [1] and **Chamberlain *et al.*** [2] (figures 1 and 2).

All patients during the study period from September 2013 until June 2014 were followed up for any reported side effect or hospitalization.

Data Analysis

Quantitative values were calculated as mean value. Frequency and percentage were calculated and presented. Data from observation were analyzed descriptively.

RESULTS

A total of 250 patients with the most common indications for warfarin were aortic and mitral valves replacement (84.4%) and atrial fibrillation (15.6%) were referred to the clinic. The target INR (2-3) was for 90 patients and the others with target INR (2.5-3.5). The range of age group of the patients was wide, 5-81 years. 65% of them were males (Table 1).

72% of the patients who referred to the clinic were not achieving therapeutic INR (TINR). 43% of them reached the TINR within the first week and28%, 17%, and 4% reached the TINR within the (2nd, 3rd, 4th weeks respectively). 8% exceeded 4 weeks (Figure 3).

The proportion of (TINR) for all patients during the whole period was 75%. 7% of the patients had low INR, <1.5 for one visit with no major thromboembolic events. 5% of the patients had high INR, >4.5 with main adverse events due to high INR were bruising and epistaxis. There were no hospitalization or emergency visits reported during the whole period of the study.

DISCUSSION

Warfarin is one of the most complex drugs prescribed worldwide, [7-10] because of the need for individualized dosing and monitoring and its narrow therapeutic range.

In this prospective observational study the impact of our newly established clinic was evaluated on patients' outcomes regarding time needed for achieving target INR, the proportion of time within therapeutic INR and finally controlling adverse events and preventing complications and hospitalization.

The first outcome which was evaluated, the time needed for achieving TINR. The patients who referred to the clinic with uncontrolled INR were 72% even they were on warfarin for two months. The majority of them (43%) reached the

TINR within the first week. While the reminders; (28%, 17%, and 4% reached the TINR within the (2nd, 3rd, 4th weeks, respectively). 8% exceeded 4 weeks. These results in line with many observational studies, which reported that the time between non-therapeutic INR values and follow-up INR testing was significantly shorter in the anticoagulation management service. **(11,12)** There are growing evidences that pharmacist managed anticoagulation clinic achieve better INR control than conventional care with regard to achieving and maintaining target INR. **(13)** So INR close monitoring is recommended to achieve the therapeutic goal as fast as possible in order to avoid significant complications due to high or low INR. The second outcome which was focused on, the proportion of time in (TINR) for all patients during the whole period. The proportion of time in therapeutic range (TTR) can be used as a measure of the quality of anticoagulation control. The greater the time within TINR, the better the balance is between the risks and benefits of warfarin treatment (Schillig et al., 2011).(16) The British Committee for Standards in Hematology (BCSH), recommend maintaining a time in TINR of 60% or above in order to maximize benefits from treatment and to limit adverse events (Baglinet al., 2006). **(17)**

The proportion of time in (TINR) for all patients in our study was 75%.Such findings have been reported previously by Thomas et al. (6), Witt et al. (11), You et al. (18), Wilson et al.(19), Ernst and Brandt(20), and Young et al. (15), the TTR were (67.9%, 63.5%, 78%, 82%, 57.8%, and 73% respectively), which are comparative to our study. As discussed early Warfarin can lead to several serious complications if not monitored closely, generally these complications are less frequent with pharmacist managed group (Shaw et al. (21). The percentages of high INR (>4.5), low INR, (<1.5) and the adverse effects due to these percentages were the third outcome of our study. 5% of the patients had high INR (>4.5). 10 patients were poor adherent (high false doses). 3 patients took Ciprofloxacin. The main adverse events due to high INR were bruising with 3 patients and epistaxis with 4 patients. No hospitalization or emergency visits were reported during the whole period of the study.

7% of the patients during the whole period had low INR <1.5 for one visit. 16 patients were poor adherent to Warfarin (miss doses). 1 patient took a lot of Vitamin K sources during the week before visit.1 patient took a new medication (Carbamezapine). There are no major thromboembolic events due to low INR.

Such outcome was studied in Thomas et al. (6), where the percentages of high and low INR were 9.4% and 22.7%, respectively.

CONCLUSION

Our newly established clinic had achieved a considerable encouraging results and feedbacks in the short period of time since had been established. The feedbacks of patients and physicians were great. Further studies comparing the anticoagulation clinic outcomes with usual medical care and evaluation of patients and physicians satisfaction are needed.

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Table 1: The Demographic Characteristics of the Patients

Variable	Number	%
Age		
18 - 60 (year)	177	70.8
> 60 (year)	62	24.8
Sex		
Male	163	65
Female	87	35
Indication of warfarin		
Atrial fibrillation (AF)	39	15.6
MHV replacement	211	84.4
Target INR		
2 – 3	90	36
2.5 – 3.5	160	64

The protocol of altering maintenance warfarin dose to achieve target INR

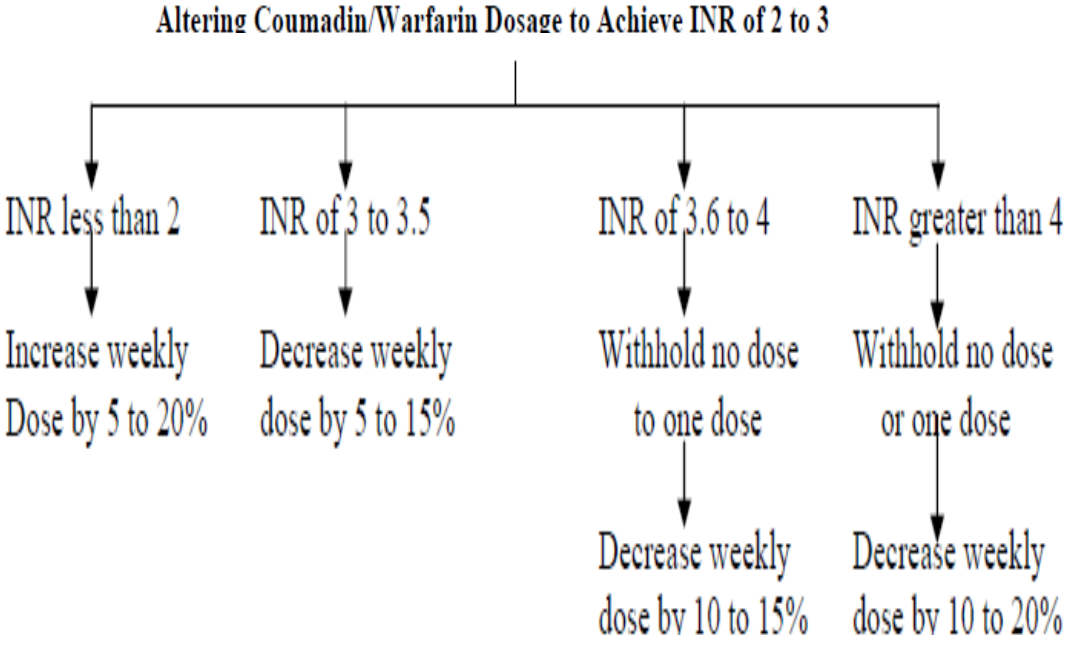

Figure 1: Warfarin Dosage to Achieve INR of 2 to3.

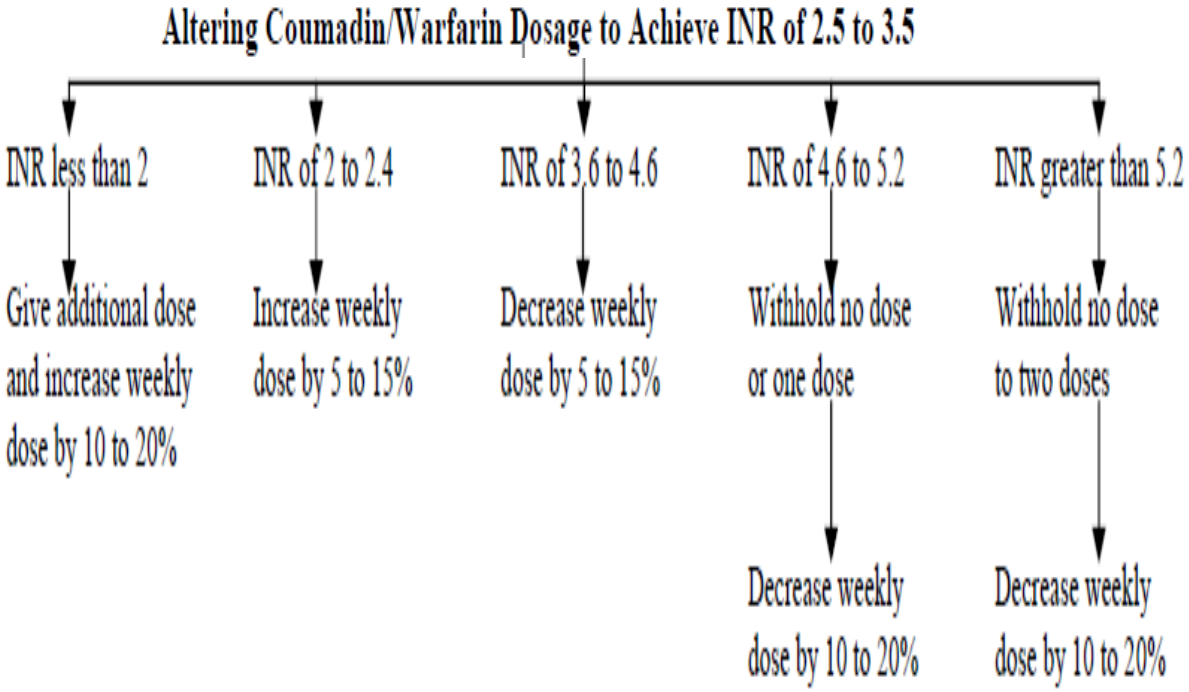

Figure 2: Warfarin Dosage to Achieve INR of 2.5 to 3.5.

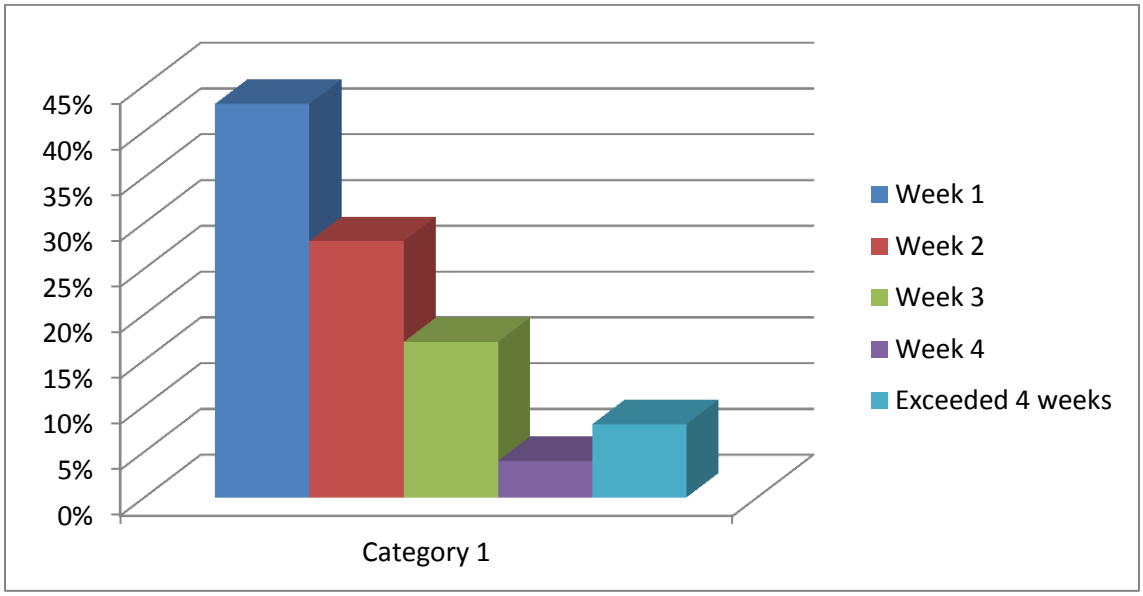

Figure (3): Time Needed To Reach (TINR)