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A STUDY OF PHARMACIST INTERVENTION IN ANTI COAGULATION CLINIC IN A TERTIARY CARE HOSPITAL, BANGLORE, INDIA

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Abstract
To assess and compare the INR results between physician (Retrospective) and clinical pharmacist dosing (Prospective) of Oral Anticoagulation drugs and to analyze the control of INR and incidence of complications during clinical pharmacist managed therapy. Data was collected using a well-structured data collection form which includes patient's demographics, clinical information which includes (indication for anticoagulation therapy, desired INR range, expected duration of therapy, anticoagulation therapy received), social habits, past medical history, current medications and the prescribed oral anticoagulant (Warfarin/Acitrom). INR values were monitored for the patients included in the study and dosage adjustment was done according to standard protocol based on the INR value. The patients were also provided with effective counseling regarding the therapy and dietary modifications. All the patients were monitored for any adverse drug events/effects or any possible drug and food interactions during the study period. In case of any reported adverse events/drug interactions in the anticoagulation clinic, proper intervention was done by the clinical pharmacist in association with physician to achieve rational drug therapy. During our study period, 86 patients were forwarded by the physicians to the clinical pharmacist managing oral anticoagulation clinic. Only 82 patients could complete the study, where 4 patients did not visit the clinic, other 12 patients did not meet the inclusion criteria and hence they are excluded. The data were collected using data collection form for the study sample. After the interventional study there was a significant improvement in patients maintaining % of INRs which were in target therapeutic range, % of TTR along with decreased adverse effects. It was also found that patient's awareness of the target INR values is correlated with the improved accuracy of anticoagulation control. Hence, our study results reflect the need for a clinical pharmacist in oral anticoagulation management and the necessity of implementing anticoagulation services in various hospital settings. The clinical pharmacist managing anticoagulation service was able to achieve the INRs of the patient in to target therapeutic range by proper and timely dose adjustments based on the INR value, to identify adverse drug reactions/ adverse events, drug-drug interactions and drug-food interactions and bring about proper interventions by working in association with physicians.

Keywords: Anticoagulant, Clinical pharmacist intervention, INR results, Physician intervention**.**

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INTRODUCTION

Anticoagulants are one of the most common drug classes involved in adverse events. Warfarin has a narrow therapeutic index and a number of challenges have been recognized in managing OAT, including the need for frequent laboratory monitoring and dose adjustment, drug and food interactions, the influence of co-morbidities on anticoagulation control [7]. Selection of the right Warfarin dose at the treatment is not straightforward, because of substantial inter-patient differences in sensitivity to Warfarin, numerous variables (patient's nutritional status, gender) that can alter the response to therapy with time, and the potential risk for major hemorrhage. A systematic approach to therapeutic drug monitoring must be carried out for every patient who has anticoagulation therapy [5].

The most serious interactions are those that increase the anticoagulant effect and the risk of bleeding. Warfarin combine 3 unfavorable properties which make them prone to potentially life threatening drug-drug interactions: high plasma protein binding, cytochrome p_{450} dependent metabolism and narrow therapeutic range [5], and also inhibition of metabolism (Amiodarone, Omeprazole, Statins), affection of bio-availability, protein binding (Digoxin, Salicylates). The potential risk associated with the use of Warfarin can be reduced by incorporating changes into the way in which anticoagulation care is delivered [7]. By using the lowest possible required dose of anticoagulant, the physician can minimize the risk of bleeding while providing the benefits of anticoagulation [5]. Good therapeutic control of VKA treatment, with regular prothrombin time (PT) tests reported as INR within intended therapeutic range (TR) is imperative for minimizing adverse events (bleeding and/or thrombosis) [8].

Anticoagulation management is a challenging task for health care professionals especially for clinical pharmacists, because of the individual variability in response to the anticoagulants, alterations in a patient's consumption of vitamin K- rich foods and alcohol, change in medications, or change in health status all of which can alter the INR values [2]. It is important to manage anticoagulation therapy of patients in a department like cardiology as many drug related problems and patient non-compliance are common and hence there is a need for better pharmaceutical care and effective care that can be provided by a clinical pharmacist [2]. Pharmacist can also bring expertise in managing oral and parenteral anticoagulation therapy of both inpatients and outpatients by providing important information regarding therapy through effective counseling and about potential interactions [3].

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Clinical pharmacists have become experienced and expertise in managing oral and parenteral anticoagulation therapy, in addition to daily dosing recommendations to attending physicians, other staffs and timely dose titrations [4]. The role of the clinical pharmacist include therapeutic monitoring, Warfarin dosage adjustment, management of Warfarin related and unrelated problems, patient counseling and education, and co-ordination of the anticoagulation clinic activities like following up of discharged patients, communicating patient progresses and problems with physician etc.[5,6]. Monitoring parameters include INR values, signs and symptoms of hemorrhagic and thromboembolic events, drug-drug interactions, drug-food interactions, drug-disease interactions and patient compliance [1]. Proper educational guidance and monitoring of the INR status regularly is the only step for the successful anticoagulation [2].

MATERIALS AND METHODS

Study design

A Bidirectional (prospective and retrospective) observational and interventional study will be conducted to include patients receiving oral anticoagulation drugs (Warfarin, Acitrom) among adult patients between December to May 2016

Inclusion criteria

Patients forwarded to anticoagulation clinic by the Physician of Age groups between 18-60 yrs. between December to May 2016 in Tertiary Care Hospital,Aster CMI Hospital,Bangalore, India.

Exclusion criteria

Patients with Severe co-morbid conditions like End stage liver damage, Kidney failure, Cancer.
Pregnancy women
Paediatric patients
Patients with psychiatric disturbances

Data Collection Method

Data was collected using a well-structured data collection form which includes patient's demographics, clinical information which includes (indication for anticoagulation therapy, desired INR range, expected duration of therapy, anticoagulation therapy received), social habits, past medical history, current medications and the prescribed oral anticoagulant (Warfarin/Acitrom).

The INR values of the study sample were collected from the hospital medical record database for 3 consecutive reviews for the physician dosing retrospectively, the PT and INR values were recorded prospectively in the clinical pharmacist managed oral anticoagulation clinic during the

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study period for the same selected patients on 3 regular follow-up's with relevant source of information. INR values were monitored for the patients included in the study and dosage adjustment was done according to standard protocol based on the INR value. The patients were also provided with effective counseling regarding the therapy and dietary modifications. All the patients were monitored for any adverse drug events/effects or any possible drug and food interactions during the study period. In case of any reported adverse events/drug interactions in the anticoagulation clinic, proper intervention was done by the clinical pharmacist in association with physician to achieve rational drug therapy.

RESULT AND DISCUSION

During our study period, 86 patients were forwarded by the physicians to the clinical pharmacist managing oral anticoagulation clinic. Only 82 patients could complete the study, where 4 patients did not visit the clinic, other 12 patients did not meet the inclusion criteria and hence they are excluded. The data were collected using data collection form for the study sample. Out of 216 INRs checked for 70 patients (total of 3 follow-ups), the target therapeutic range was found to be 100 (45.78%) and 140 (64.25%) respectively for physician and clinical pharmacist dosing. Our study results showed a significant increase in target INR values during the period of clinical pharmacist managing oral anticoagulation therapy. The paired sample t-test was used to compare target INR values in the physician and clinical pharmacist managed groups. Table No 1 shows the corresponding p-values of the INRs within the target range, sub therapeutic range and supra therapeutic range is less than the significance value 0.01. Hence, we conclude that our study is statistically significant at 1%.

Table 1: Paired sample t-test for comparison of INR results in Physician and Clinical Pharmacist intervention

INR results	Differences of the Mean	Paired t-value	Degree of Freedom	P-value
INRs in target value	-0.6642	4.803	82	< 0.0001
INRs > target value	0.1646	2.541	82	0.0088
INRs < target range	0.3002	2.608	82	0.0044
INRs > 5	0.07229	1.228	82	0.1114
INRs < 1	0.03814	1.398	82	0.1813

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Table 2 and 3 shows the evaluation of the frequency and cause of oral anticoagulant related adverse effects/ events are mainly due to lack of knowledge regarding anticoagulation therapy, irregular follow-up and unavailability of 0.5mg of Acitrom and concurrent administration of other drugs. Some of the occurred events were taken to the knowledge of physician for further management where as in remaining patients dose adjustment was done according to the standard protocol of oral anticoagulation therapy along with effective counseling.

Our study results are also supported by the Gregory Piazza *et al.*, who conducted this similar study in anticoagulation – associated adverse events [3].

Apart from the above, drug and food interactions were also observed in few patients receiving oral anticoagulation therapy which was depicted in Table 4.

Table 2: Adverse Drug Event Occurred in Anticoagulation Clinic (for Sub therapeutic INR (< 2))

Enrolling anti-coagulation clinic	Drug	Adverse event	Hospitalized	Cause	Clinical Pharmacist Intervention	Outcome
Yes	Acitrom	Chest tightness, Upper body discomfort	No	Missed follow-up	Dose adjustment done	Recovered
Yes	Acitrom	Tenderness in shoulder Joints	No	Took Hopace (Ramipril) Thinking as Acitrom	Counseled the patient about the drug	Recovered
Yes	Acitrom	Chest tightness	No	Took 2MG Instead of 2.5Mg(due to unavailability of (0.5mg) at Hospital Pharmacy	Dose adjusted	Recovered
Yes	Acitrom	Chest tightness	No	Patient Stopped Drug By Tappering the Dose And Tried to Manage by yoga (not took drug)	Counseled the patient about the Disease And Therapy	Recovered

Table 3 Adverse Drug Event Occurred in Anticoagulation Clinic (for Supra therapeutic INR (> 5))

Enroll anti-coagulation clinic	Drug	Adverse event	Hospital-ized	Cause	Clinical Pharmacist Intervention	Outcome
Yes	Acitrom	Haematuria	Yes	Took 8mg instead of 4mg	Informed to Physician	Recovered
Yes	Warfarin	Tongue Bleeding	Yes	Took NSAID's	Informed to Physician	Recovered

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Yes	Warfarin	Bleeding Stools	Yes	Missed Follow up with anticoagulation clinic	Informed to Physician Hb-6gm/dl	Transfused, Recovered
Yes	Warfarin	Black colour stool	Yes	Irregular follow-up	Informed to physician	Recovered
Yes	Acitrom	Haematuria	Yes	Unknown cause	Informed to physician	Recovered

Most of the patients received useful information from an anticoagulation service and the convenience, accessibility, and services provided by the clinical pharmacist were better.

This was assessed by questioning patients/caretakers answering a set of satisfaction assessment questionnaire [3] and about satisfaction was reported in the present study.

Table 4: Drug and Food Interactions observed in study sample

	Interacting agents	**Drug**	**Interactions**	**No of occurrence**	**Clinical Pharmacist intervention**
Drug Interaction	Tegritol (Carbamazepine)	Warfarin	Increased anticoagulation effect	1	Informed to physician and regimen was changed to Epilive(Levetiracetam)
	Trapic-MF (Tranexamic Acid)	Warfarin	Increased anticoagulation effect	1	Patient Counseled not to take OTC medications and to consult physician on any disability and inform the physician about the anticoagulant drug
Food Interactions	Green Tea	Warfarin(3) /Acitrom(2)	Decreased INR	3	Patient Information given on interaction of green tea with the drug

After the interventional study there was a significant improvement in patients maintaining % of INRs which were in target therapeutic range, % of TTR along with decreased adverse effects. It was also found that patient's awareness of the target INR values is correlated with the improved accuracy of anticoagulation control. Hence, our study results reflect the need for a clinical pharmacist in oral anticoagulation management and the necessity of implementing anticoagulation services in various hospital settings.

CONCLUSION

Due to increased number of patients receiving OAT it is quite difficult for the physician to educate all the patients due to lack of time. From our study we concluded that the clinical pharmacist managing anticoagulation service was able to achieve the INRs of the patient in to target therapeutic range by proper and timely dose adjustments based on the INR value, to identify adverse drug reactions/ adverse events, drug-drug interactions and drug-food interactions and bring about proper interventions by working in association with physicians. Poor doctor-

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patient communication can also be overcome by the involvement of clinical pharmacist in anticoagulation management through effective counseling regarding the medication, importance of monitoring INR values, life style and dietary modifications. Moreover clinical pharmacist can also act as good communicators between physicians and patients.

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