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ROLE OF CLINICAL PHARMACIST IN ANTI - COAGULATION CLINIC TOWARDS BETTER PATIENT CARE IN A TERTIARY CARE HOSPITAL

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Abstract: Many reports have documented the ability of anticoagulation management services by clinical pharmacist to help patients receiving oral anticoagulation in order to achieve better therapeutic outcomes. The present Bidirectional, Observational and Interventional study was carried out in clinical pharmacist managed oral anticoagulation clinic in a tertiary care hospital for a period of 6 months to evaluate the effectiveness of clinical pharmacist. The clinical pharmacist in the anticoagulation clinic had taken the responsibilities like dose adjustment, management of oral anticoagulants related and unrelated problems including ADR monitoring, interaction checking and sorting out it to physician, effective patient counselling, providing information leaflets, determining Time in Therapeutic Range (TTR) and assessing patient satisfaction towards oral anticoagulation clinic. Clinical outcomes were measured at the end of the study which showed there was statistically significant improvement in maintenance of target INR value in patients monitored by clinical pharmacist (Prospective) when compared to physician (Retrospective). The fraction of INRs within therapeutic range indicated better anticoagulation control in clinical pharmacist group when compared to physician group (0.642 vs 0.457). The study showed the importance of clinical pharmacist in anticoagulation clinic in achieving better outcome in patients receiving oral anticoagulants as evidenced by the increase in the values of target INR, TTR and hence showed better anticoagulation control.

Keywords: Oral Anticoagulation Clinic, Clinical Pharmacist, Oral Anticoagulants, INR, Satisfaction.



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INTRODUCTION

Anticoagulation clinics/services are established to monitor and manage the medications that are used by the patients to prevent blood clots ⁽¹⁾ and Clinical pharmacist in anticoagulation clinic can easily understand complications, etiopathogenesis and quickly provide specific therapeutic interventions in emergency conditions ⁽²⁾. Coumarinic oral-anticoagulants (COA) like Warfarin, Acenocoumarol and Phenprocoumon are most frequently prescribed drugs for managing problems associated with blood coagulation in patients with Atrial fibrillation (AF), Heart valve replacement (HVR), Deep vein thrombosis (DVT), Pulmonary embolism (PE) and patients who had undergone Orthopaedic surgery. COA therapy is usually given lifelong and its dosing management is very difficult due to its Narrow therapeutic index and there are also significant inter individual differences as well as interethnic differences in stabilizing dosage ⁽³⁾. Warfarin is considered as the mainstay of oral-anticoagulant therapy for the past sixty years ⁽⁴⁾ and it is the first line drug in North America, Scandinavia, and Great Britain. Although unavailable in United States of America most European countries, including Germany are using Acenocoumarol as the first line drug whereas in other parts of the Europe and elsewhere, Acenocoumarol is often used as alternative drug to Warfarin ⁽⁵⁾. Most of the studies relating anticoagulation clinics and clinical pharmacist role are based on the perspective of the western countries. In the developing country like India such studies would be worthwhile to demonstrate the improvement the quality of care and can justify the need for such services with respect to the growing service needs of patients and lead to development of such patient friendly services in hospitals ⁽⁶⁾. The number of patients on OAT is steadily increasing worldwide ⁽⁷⁾. Anticoagulants are also 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 ⁽⁸⁾. Other factors including diet, alcohol, other medications, illness and adherence can adversely affect the safety and efficacy of Warfarin ⁽⁹⁾. 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) ⁽¹⁰⁾. The safe management of oral anticoagulation in patients is a challenge in both ward and community. Sub-therapeutic and Supra-therapeutic INR can be hazardous to the patient ⁽¹¹⁾. Hence clinical pharmacists have been shown to effectively manage anticoagulation therapy through maintaining INR's within therapeutic range and thereby lowering the incidence of adverse events, drug interactions and other possible risks ⁽¹⁾. Successful anticoagulation treatment is dependent on the patient's knowledge of drug ⁽⁷⁾. Drug compliance and anticoagulation control provides patient education which becomes the part of the management plan ⁽⁶⁾.

MATERIALS AND METHODS:

Design of study: A Bidirectional (prospective and retrospective) Observational and Interventional study was conducted to include patients receiving oral anticoagulation drugs (Warfarin, Acitrom) among adult patients from February 2014 to June 2014.

Study site: A tertiary care hospital in Coimbatore, Tamil Nadu, India.

Sample size: A sample size of 83 patients was included in the study for testing the hypothesis.

Inclusion criteria: Patients forwarded to anticoagulation clinic by the Physician of Age groups between 18-58yrs.

Exclusion criteria: Patients with Severe co-morbid conditions like End stage liver damage, Kidney failure, Cancer, Pregnancy women, Pediatric patients and patients with psychiatric disturbances.

Methodology: 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 of the physician dosing retrospectively, the PT and INR values were recorded prospectively in the clinical pharmacist managed oral anticoagulation clinic during the 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.

The comparison of the INR values and TTR (Rosendaal method) in the patients was analyzed between the physician and clinical pharmacist managed oral anticoagulation therapy and the outcomes were evaluated. 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.

The information was collected regarding all the cases met the inclusion criteria and the data was recorded in MS Excel sheet. Data analysis was done with the help of computer using graph pad. Using this, means, Differences of means, percentages, degree of freedom, sample paired t test, were calculated. A 'p' value less than 0.01 is taken to denote significant relationship. Time in Therapeutic range was calculated using Rosendaal method of linear interpolation and the obtained values were summarized in to percentages to compare the efficacy of results.

RESULTS AND DISCUSSION:

Anticoagulation management is one of the challenging tasks for the health care providers especially for the clinical pharmacist. It is because of the inter-individual variability in response to the oral anticoagulant therapy, alterations in patient's consumption of vitamin K rich foods, alcohol consumption and changes in medications due to various co-morbidities or change in health status of which can alter the desired INR values ⁽⁶⁾. So, proper educational guidance and frequent monitoring of the INR values and dose adjustment accordingly is the only step to attain rational anticoagulation therapy. Several ^(12, 13, 14, 15, 16) studies have showed the effectiveness of clinical pharmacist managing anticoagulation in outpatient and inpatient settings. Anticoagulation management service is to monitor INR values and to adjust dose of one's anticoagulant medications for the period of time in which they need to be on anticoagulation therapy. These services are usually provided by the clinical pharmacists, which helps in assisting physicians.

During our study period, 95 patients were forwarded by the physicians to the clinical pharmacist managing oral anticoagulation clinic. Only 83 patients could complete the study, where 4 patients did not visit the clinic, other 9 patients did not meet the inclusion criteria and hence they are excluded. The data were collected using data collection form for the study sample.

The tables 1 below describes the distribution of gender, age, educational status, co-morbidities, various indications for oral anticoagulation and recommended target INRs respectively.

Table 1: Socio-Demographic details of study sample:

Sex	No. of patients	Percentage
Male	40	48%
Female	43	52%

Age distribution:

18-30 years	6	7.2%
31-40 years	13	15.6%
41-50 years	24	28.91%
51-58 years	40	48.19%
Educational status:		
Literates	36	43.4%
Illiterates	47	56.6%
Co-morbidities:		
Hypertension	38	
Heart Disease	39	
Diabetes Mellitus	13	
Thyroid disorder	6	
Asthma / COPD	3	
Stroke	2	
Respiratory Tract Infection (RTI)	2	
Peptic Ulcer/AGE	4	
Others	11	

Table 2: Indications for oral anti-coagulation

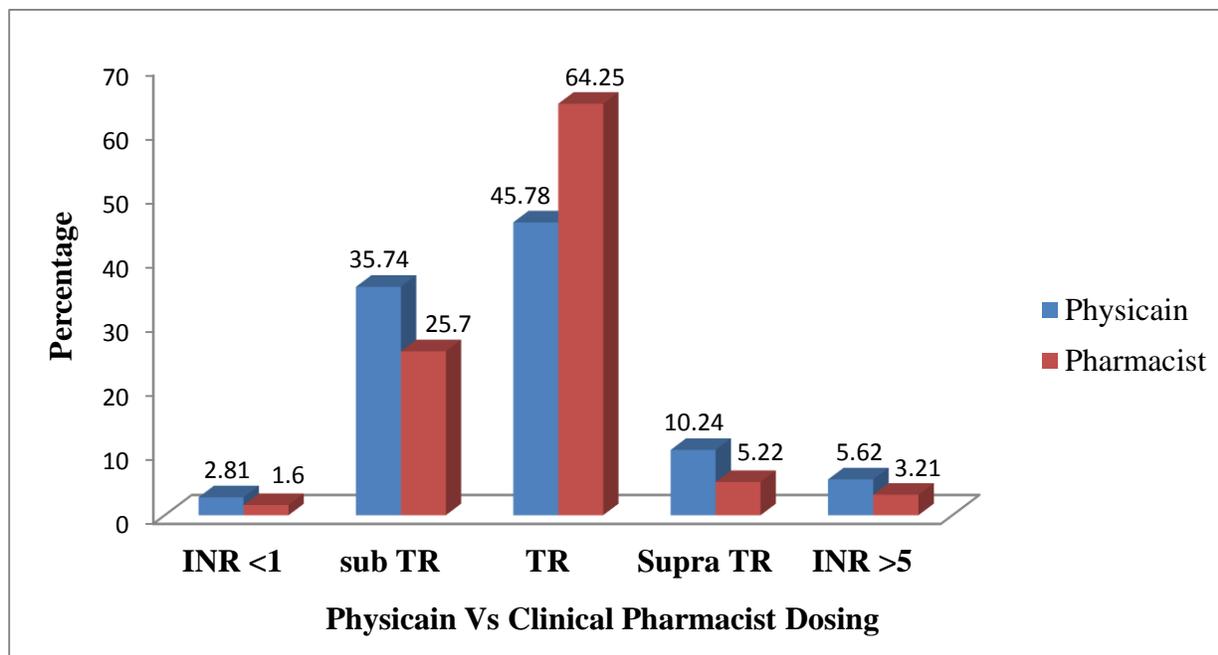
Indications	No. of patients	% of patients
Mitral Valve Replacement (MVR)	32	38.5
Atrial Fibrillation (AF)	14	16.9
Deep Vein Thrombosis (DVT)	11	13.3
Aortic Valve Replacement (AVR)	10	12.0
Pulmonary Embolism (PE)	8	9.6
MVR+AF	5	6.0
DVT + PE	1	1.2
Femoral Embelectomy	1	1.2
Ectatic Coronaries	1	1.2

Table 3: Indications and Recommended Target INR

Indications	Target INR	No. of patients	%
MVR,DVR,AF+MVR	2.5-3.5	45	54.21%
AF,AVR,DVT+PE, Femoral Embelectomy, Ectatic Coronaries	2-3	38	45.78%
TOTAL		83	100%

In our study group, out of 83 patients receiving oral anticoagulant drugs, no. of patients managed with Warfarin and Acitrom was found to be 38 (45.12%) & 45 (54.87%) respectively.

Out of 249 INRs checked for 83 patients (total of 3 follow-ups), the target therapeutic range was found to be 114 (45.78%) and 160 (64.25%) respectively for physician and clinical pharmacist dosing as shown in graph 1. Our study results showed a significant increase in target INR values during the period of clinical pharmacist managing oral anticoagulation therapy. Similar results were found in the study carried out by Nadia A Amruso ⁽¹⁷⁾.



A growing numbers of reports ^(15, 18, 19, 20) have suggested that implementing an anticoagulation management service helps in achieving better patient clinical outcomes when compared to the usual care provided by the physicians. The fraction of INRs within therapeutic range was found

to be 0.457 and 0.642 for physician dosing (Retrospective) and clinical pharmacist dosing (Prospective) groups respectively for the present study which showed a significant increase in a clinical pharmacist managed oral anticoagulation clinic which helps in optimizing patient care towards oral anticoagulation therapy with the help of anticoagulation clinic. (Table 4)

Table 4: Fraction of INRs in the therapeutic range for the study sample

INR results	Physician	Clinical pharmacist
Total INR's checked	249	249
INR's within TR	114	160
Fraction of INR within TR	0.457	0.642

The paired sample t-test was used to compare target INR values in the physician and clinical pharmacist managed groups. Table no.5 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 5: Paired sample t-test for comparison of INR results in Physician and Clinical Pharmacist intervention:

INR results	Differences of Mean	Paired t-value	p value
INRs in target range	-0.5542	4.703	<0.0001
INRs > target value	0.1446	2.421	0.0088
INRs < target range	0.3012	2.688	0.0044
INRs >5	0.7229	1.228	0.1114
INRs <1	0.03614	1.348	0.1813

p value < 0.01 is significant

Time in therapeutic range (TTR) is an estimate of the number of days that a patient has a desired INR range with in their duration of anticoagulant therapy received. ⁽²¹⁾. Hence, TTR is considered as the standard for the monitoring of oral anticoagulation therapy. In our study we used Rosendaal method of linear interpolation to determine TTR of both physician and clinical

pharmacist's dosing period for the entire study sample (n=83) who met the inclusion criteria and obtained the TTR value of 54.12% and 64.85% respectively. Similar study *Jennifer Rossiter et al.*,⁽²¹⁾ also supports the improvement in time in therapeutic range while receiving anticoagulation therapy by the clinical pharmacist.

Cumulative number of days observed for two consecutive follow-ups of the study sample.

Table 6: Evaluation of TTR.

TTR	Physician (No. of days)	Clinical Pharmacist (No. of days)
Stable Treatment	5250 (54.12%)	3820 (64.85%)
Out of Therapeutic Range	4449 (45.87%)	2070 (35.14%)
Total	9699	5890

Table No.7 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⁽²²⁾. Apart from the above, drug and food interactions were also observed in few patients receiving oral anticoagulation therapy which was depicted in Table

Table 7: Adverse Drug Event Occurred in Anticoagulation Clinic

Patient	Enrolling anti-coagulation clinic	Drug	Adverse event	Hospit-alized	Cause	Clinical Pharmacist Intervention	Outcome

Sub therapeutic INR (< 2)

1	Yes	Acitrom	Chest tightness, Upper body discomfort	No	Missed follow-up	Dose adjustment done	Recovered
2	Yes	Acitrom	Tenderness in shoulder Joints	No	Took Hopace (Ramipril) Thinking as Acitrom	Counseled the patient about the drug	Recovered
3	Yes	Acitrom	Chest tightness	No	Took 2MG Instead of 2.5Mg(due to unavailability of (0.5mg) at Hospital Pharmacy	Dose adjusted	Recovered
4	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

Patient	Enrolling anti-coagulation clinic	Drug	Adverse event	Hospital-ized	Cause	Clinical Pharmacist Intervention	Outcome
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Supra therapeutic INR (> 5)

5	Yes	Acitrom	Haematuria	Yes	Took 8mg instead of 4mg	Informed to Physician	Recovered
6	Yes	Warfarin	Tongue Bleeding	Yes	Took NSAID's	Informed to Physician	Recovered
7	Yes	Warfarin	Bleeding Stools	Yes	Missed Follow up with anticoagulation clinic	Informed to Physician Hb-6gm/dl	Transfused, Recovered
8.	Yes	Warfarin	Black colour stool	Yes	Irregular follow-up	Informed to physician	Recovered

9.	Yes	Acitrom	Haematuria	Yes	Unknown cause	Informed to physician	Recovered
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Table 8: Drug and Food Interactions observed in study sample

	Interacting agents	Drug	Interactions	No of occurrence	Clinical intervention	Pharmacist
Drug Interaction	Tegritol (Carbamazepine)	Warfarin	Increased anticoagulation effect	1	Informed to physician and regimen was changed to Epilive (Levetiracetam)	
	Traptic-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 anticoagulants	
Food Interactions	Green Tea	Warfarin (3) /Acitrom (2)	Decreased INR	5	Patient Information given on interaction of green tea with the drug	

Table 9: Patient Feedback on Anticoagulation Clinic

S.NO	QUESTION	RESPONSE	
		YES	NO
1.	Are you satisfied with the follow-up arrangements by the anticoagulation management service?	83	0
2.	Did you find any problems associated with the follow-up arrangements?	5	78

3.	Are you satisfied with the counseling provided by clinical pharmacist?	83	0
4.	Were the written information booklet provided easy to read and understand?	77	6

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 questioning patients/caretakers answering a set of satisfaction assessment questionnaire (23) and about satisfaction was reported in the present study. Similar studies Lakshmi R et al., (23) also support the fact of patient satisfaction by the anticoagulation service offered by clinical pharmacist.

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.

LIMITATIONS OF THE STUDY:

The total numbers of patients forwarded to the OAC by the physician were not able to be followed because of irregular visits of the patients. It is not possible to take in to account about the natural fluctuations in INR was another limitation.

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-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.

Thus anticoagulation clinic laid a foundation in building good relationship between physician, clinical pharmacist and patients. Since, clinical pharmacist can effectively manage anticoagulation therapy and provide optimal care to the patients and there is a strong need for clinical pharmacist in anticoagulation clinic in health care setup which will empower patients to improve quality of care and to achieve better therapeutic outcome with improved safety in patients who receives oral anticoagulation therapy.

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