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ORIGINAL ARTICLE

Prescribing Pattern and Pharmacist Intervention in Anticoagulation at A Tertiary Care Teaching Hospital, Coimbatore, India

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ABSTRACT

Objective: To assess the prescribing pattern and pharmacist intervention in anti-coagulation at a tertiary care teaching hospital, Coimbatore, India

Methodology: Data was gathered utilizing a well-structured data collection structure which includes patient's demographics, clinical data which includes (indication for anticoagulation therapy, wanted INR range, anticipated length of therapy, anticoagulation therapy got), social propensities, past medical history, current prescriptions and the prescribed oral anticoagulant (Warfarin/Acitrom). INR values were observed for the patients remembered for the investigation and dosage adjustment was finished by standard convention dependent 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 associations in the anticoagulation facility, the legitimate intervention was finished by the clinical pharmacist in relationship with a physician to accomplish objective drug therapy.

Result: During our study period, 86 patients were forwarded by the physicians to the clinical pharmacist managing the oral anticoagulation clinic. Only 70 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 the 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: 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,

INTRODUCTION

Anticoagulants are a class of drugs that work to prevent blood coagulation (clotting). Anticoagulants are closely related to antiplatelet and thrombolytic drugs by manipulating the various pathways of blood coagulation. Anticoagulation clinics/services are established to monitor and manage the medications that are used by the patients to prevent blood clots [(1)] and Clinical pharmacists in the anticoagulation clinic can easily understand complications, etiopathogenesis and quickly provide specific therapeutic interventions in emergency conditions [(2)].

Coumarin oral anticoagulants (COA) like Warfarin, Acenocoumarol, and Preprohormone are most oftentimes prescribed drugs for overseeing issues related to blood coagulation in patients with Atrial fibrillation (AF), Heart valve replacement (HVR), Deep vein apoplexy (DVT), Pulmonary embolism (PE) and patients who had gone through Orthopedic medical procedure. In North India, Acenocoumarol is broadly utilized rather than Warfarin. COA therapy is typically given deep-rooted and its dosing management is exceptionally troublesome because of its Narrow remedial list and there are significant inter-individual contrasts just as interethnic contrasts in stabilizing dosage [(3)].

Comparative studies of vitamin k antagonists, Warfarin, and Acenocoumarol are rare, probably due to their geographical distribution according to which certain regions use only Warfarin while other regions use only Acenocoumarol (Acitrom). Warfarin is considered the first-line drug in North America, Scandinavia, and Great Britain. Although unavailable in the United States of America most European countries, including Germany, are using Acenocoumarol as the first-line drug whereas in other parts of Europe and elsewhere, Acenocoumarol is often used as an alternative drug to Warfarin [(4)].

Despite the continuously growing number of patients with Atrial fibrillation and the increased possibility of developing other cardiac problems, the usage of more specific and potentially more stable oral-anticoagulants like Warfarin and Acenocoumarol is still increasing. These drugs are in the top hundreds of the most prescribed drugs in the world [(4)].

Most of the studies relating to anticoagulation clinics and clinical pharmacist roles are based on the perspective of western countries. In a developing nation like India, such investigations would be beneficial to show the improvement of the quality of mind and can legitimize the requirement for such administrations concerning the developing help needs of patients and lead to the advancement of such patient well-disposed administrations in hospitals [(5)].

Clinical pharmacists have gotten experienced and skill in overseeing oral and parenteral anticoagulation therapy, as well as every day, dosing suggestions to going to physicians, different staffs, and ideal portion titrations [7]. The job of the clinical pharmacist includes therapeutic monitoring, Warfarin dosage adjustment, management of Warfarin related and random issues, patient guiding, and training, and co-appointment of the anticoagulation facility exercises like after up of released patients, imparting patient progress and issues with a physician, etc. [6]

Monitoring boundaries incorporate INR values, signs and manifestations of hemorrhagic and thromboembolic events, drug-drug interactions, drug-food interactions, drug-infection interactions, and patient consistency [4]. Legitimate instructive direction and monitoring of the INR status consistently is the lone advance for successful anticoagulation [5].

Considering, advantages provided by an OAC an integration between hospital administrations and primary care units is alluring to normalize the quality of treatment on anticoagulation [2] by determining the appropriate clinical indications for anticoagulant treatment, choosing the best drug concerning clinical patient profile, evaluating any potential pharmacological interference, in particular in the elderly, defining a follow-up program through educational programs to increase drug adherence, managing patients with bleeding, intercurrent diseases and thrombotic complications, during anticoagulant treatment. Educational courses for patients (indication for treatment, risk, and benefit, problem in the drug administration, dietary behavior, interactions with other drugs, and intercurrent disease) and health territories care units can improve patient's compliance [2].

Anticoagulation management is one of the challenging tasks for health care providers, especially for the clinical pharmacist. It is a result of the inter-individual variability in light of the oral anticoagulant therapy, adjustments in patient's utilization of vitamin K rich food varieties, liquor utilization, and changes in prescriptions because of different co-morbidities or change in wellbeing status of which can modify the ideal INR values [5]. Along these lines, legitimate instructive direction and incessant monitoring of the INR values and portion adjustment as needs be is the lone advance to achieve rational anticoagulation therapy. A few [8-12] studies have shown the adequacy of clinical pharmacists overseeing anticoagulation in outpatient and inpatient settings. Anticoagulation management administration is to screen INR values and to change the portion of one's anticoagulant meds for the timeframe in which they should be on anticoagulation therapy. These administrations are generally provided by clinical pharmacists which helps in helping physicians. [13-14]

The most serious interactions are those that increase the anticoagulant effect and the risk of bleeding. Warfarin combines 3 unfavorable properties which make them inclined to conceivably life-threatening drug-drug interactions: high plasma protein binding, cytochrome p450 dependent metabolism and narrow therapeutic range [15], 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 how anticoagulation care is delivered [17]. By utilizing the lowest possible required portion of anticoagulant, the physician can limit the risk of draining while at the same time giving the advantages of anticoagulation (16). Great therapeutic control of VKA treatment, with standard prothrombin time (PT), tests detailed as INR inside planned therapeutic reach (TR) is basic for limiting adverse events (draining as well as apoplexy) (18).

METHODOLOGY

Data was gathered utilizing a well-structured data collection structure which includes patient's demographics, clinical data which includes (indication for anticoagulation therapy, wanted INR range, anticipated length of therapy, anticoagulation therapy got), social habits, past medical history, current meds, and the prescribed oral anticoagulant (Warfarin/Acitrom). The INR values of the investigation test were gathered from the hospital medical record database for 3 continuous surveys for the physician dosing retrospectively, the PT and INR values were recorded

prospectively in the clinical pharmacist oversaw oral anticoagulation facility during the examination time frame for similar chose patients on 3 customary follow-ups with the applicable wellspring of data. INR values were observed for the patients remembered for the investigation and dosage adjustment was finished by standard protocol dependent 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 the event of any revealed adverse events/drug interactions in the anticoagulation center, the appropriate intervention was finished by the clinical pharmacist in relationship with the physician to accomplish rational drug therapy.

RESULT AND DISCUSSION

The study period was 180 days. All the inpatients to the critical care units as per the inclusion criteria have been studied for current data. The study population consisted of 70 patients observed during the same 121 days of the observation period. Out of which, 70 were male patients 34(48%) and 36(52%) were female.

Out of 216, INRs checked for 70 patients (total of 3 follow-ups), the objective therapeutic reach was discovered to be 100 (45.78%) and 140 (64.25%) individually for physician and clinical pharmacist dosing. Our investigation results showed a significant expansion in target INR values during the time of clinical pharmacists overseeing oral anticoagulation therapy. Table 1

A growing number of reports [14, 28, 31, 32] 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 inside therapeutic reach was discovered 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. Table2, 3,

The paired sample t-test was used to compare target INR values in the physician and clinical pharmacist-managed groups. Table4 shows the corresponding p-values of the INRs within the target range, sub-therapeutic range, and supratherapeutic range is less than the significance value 0.01. Hence, we conclude that our study is statistically significant at 1%.

Table 1: Indications for Oral Anticoagulation in the study sample

Indications	No. of patients	% of patients
Mitral Valve Replacement (MVR)	32	38.55
Atrial Fibrillation (AF)	12	16.86
Deep Vein Thrombosis (DVT)	10	13.25
Aortic Valve Replacement (AVR)	8	12.04
Pulmonary Embolism (PE)	6	9.63
Mitral Valve Replacement MVR + Atrial Fibrillation AF	2	6.02
Total	70	100%

Table 2: Management of patients with Oral Anticoagulation drugs

Management	No. of Patients	% of Patients
Warfarin	30	45.12
Acitrom	40	54.87
Total	70	100

Table 3: Physician Vs Clinical Pharmacist Dosing

INR Results	Physician Dosing (Retrospective)[No. (%)]	Clinical Pharmacist Dosing (Prospective)[No. (%)]
INRs within a target range	100(45.78)	140 (64.25)
INRs above target range	25 (10.04)	13 (5.22)
INRs below target range	80 (35.74)	51(25.70)
INRs >5	14 (5.62)	08 (3.21)
INRs<1	07 (2.81)	04 (1.6)
Total INRs checked	216	216

Table 4: 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

p value < 0.01 is significant

Table 5: Adverse Drug Events Occurred in Anticoagulation Clinic

Patient	Enrolling anti-coagulation clinic	Drug	Adverse event	Hospitalized	Cause	Clinical Pharmacist Intervention	Outcome
Subtherapeutic 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 Hop ace (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
Supra therapeutic INR (> 5)							
5	Yes	Acitrom	Hematuria	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 color stool	Yes	Irregular follow-up	Informed to physician	Recovered
9	Yes	Acitrom	Hematuria	Yes	Unknown cause	Informed to physician	Recovered

Table 6: Drug and Food Interactions observed in the 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	The patient Counseled not to take OTC medications and to consult a 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 is given on the interaction of green tea with the drug

Table No.5 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 the physician for further management whereas 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 Gregory Piazza *et al.,* who conducted this similar study in anticoagulation–associated adverse events [(19)]. Apart from the above, drug and food interactions were also observed in few patients receiving oral anticoagulation therapy which was depicted in Table No.6.

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 likewise tracked down that the patient's attention to the objective INR values is connected with the improved precision of anticoagulation control.

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CONCLUSION

Due to the 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 pharmacists in anticoagulation management through effective counseling regarding the medication, the importance of monitoring INR values, lifestyle, and dietary modifications. Moreover, clinical pharmacists can also act as good communicators between physicians and patients.

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