

CLINICAL PHARMACIST GOVERNED ANTICOAGULATION SERVICE IN STROKE UNIT OF A TERTIARY CARE TEACHING HOSPITAL

K N ANILA^{1*}, J EMMANUEL²

¹Department of Pharmacy Practice, Amrita School of Pharmacy, Amrita VishwaVidyaapeetham, AIMS Health Care Campus, AIMS, Ponekkara P.O, Kochi, Kerala, ² Professor/HOD, pharmacy practice dept., Amrita school of pharmacy Kochi, Kerala.
Email: pravinana.p@gmail.com

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ABSTRACT

Many reports have documented the ability of anticoagulation management services by clinical pharmacist to help patients receiving anticoagulants especially warfarin therapy achieves better outcomes. The present prospective and interventional study was carried out in stroke inpatient department of a tertiary care teaching hospital for a period of one year. The clinical pharmacist in the anticoagulation service had taken over the responsibilities like therapeutic drug monitoring of all patients of stroke ward, warfarin dosage adjustment in direct and via telephonic calls, management of warfarin related and unrelated problems including ADR monitoring and interaction checking and sorting out it, patient knowledge assessment using a set of validated questionnaires, patient counseling, providing information leaflets etc. Clinical outcomes were measured at the end of study. The establishment of anticoagulation clinic in the hospital helped the Stroke unit in bringing their patients under targeted anticoagulation. It helped in improving patient's knowledge compliance, reducing incidence of interactions and adverse effects. A value $p < 0.05$ indicated the significant improvement in the patient's knowledge on oral anticoagulation by clinical pharmacist interventions. Thus clinic laid a foundation in building good and healthy relation between physician, pharmacist and patients.

Keywords: Clinical pharmacist, anticoagulation services, patient knowledge, oral anticoagulants

INTRODUCTION

Anticoagulation Clinics/Services are established to monitor and manage the medications that are used by the patients to prevent blood clots¹. Clinical pharmacists have been shown to effectively manage anticoagulation therapy through a significantly higher incidence of INRs (International normalized ration) within therapeutic range and thereby lowering the incidence of adverse events, drug interactions and other possible risks². Anticoagulants like heparin and warfarin are used for the management of thromboembolic disorders and the prevention of its subsequent recurrence. They play a major role in the prevention of blood clot formation in high risk patients following surgery and in patients with prosthetic heart valves, atrial fibrillation, unstable angina or endogenous clotting disorders. Therapeutic use of heparin or vitamin K antagonists like warfarin requires individualization of the dose based on clinical indication, the patient's weight, and laboratory results. Sub therapeutic dosing can be associated with dangerous therapeutic failure or embolization, while excess dosing can cause potentially fatal bleeding. Significant side effects occurring during treatment are likely to impose a significant burden on patients and their family (e.g. frequent monitoring, side effects, monetary burden etc.) and thereby affect their health-related quality of life³. The rate of complications can be greatly reduced when health professionals and patients/caregivers have a better understanding of how to monitor and adjust warfarin therapy and how to anticipate potential problems⁴. Clinical pharmacists have become experienced and expertised in managing oral and parenteral anticoagulation therapy of both inpatients and out patients by providing important information regarding therapy through effective counseling and about potential interactions, in addition to daily dosing recommendations to attending physicians, other staffs and timely dose titrations⁵. Thus pharmacist can manage effectively both inpatients and outpatients. 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.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 compliance⁷.

METHODOLOGY

Design of study-Prospective, Interventional study.

Duration of study

The study was designed for a period of one year in which data collection was done for a period of 8 months from 1st September 2011 to 30th April 2012.

Settings

Study was carried out in the stroke inpatient department of a 1250 bedded tertiary care, teaching and super-speciality referral hospital.

Sample size

A sample size of minimum 43 patients was required for testing the hypothesis. All 43 patients who were admitted and prescribed anticoagulants oral, parenteral or both to the department of stroke medicine during the study period, who satisfied the study criteria and agreed to participate in the study were included.

Inclusion criteria

Patients under all age groups including paediatric and geriatric who were prescribed anticoagulants oral, parenteral or both and who provided necessary information in the data collection form.

Exclusion criteria

Pregnant patients, patients with severe renal insufficiency or active liver disease, and those who cannot provide necessary information in data collection form.

Methodology

Ethical clearance was obtained from the hospital ethical committee. Patient data relevant to the study were obtained by personnel interview with patients or caregivers, responding to questionnaires given for answering, examination of patient's medical record. Patient information sheet was given to the patients to let them know about the study behaviour and an informed consent was obtained from the

patient and/or patient's care givers before interviewing them. A standardized data collection form was prepared and necessary data

like demographics, indication for anticoagulation, INR lab results, dose of anticoagulants etc. were obtained from patients and/or patient's caregivers. Patient's baseline knowledge was assessed using a validated questionnaire questionnaire i.e. Oral Anticoagulation Knowledge questionnaire (OAK questionnaire of Zeolla MM, Brodeur MR, Dominelli A, Haines ST, Allie N). Scores 1 and 0 were given for each right and wrong answer. All patients and their care givers were counseled on anticoagulation therapy and its importance, common ADRs (Adverse drug reactions) and management, importance of patient compliance, dose titration, dietary modifications, and the need for INR monitoring by the clinical pharmacist. Parenteral anticoagulants were monitored for the correctness of dosing and their indication. The medical record of the patient was reviewed for any potential drug interactions and appropriate intervention was done during the ward rounds with doctors. Patients or their caregivers in the intervention group were given the contact number (oncall phone number) of clinical pharmacist to report INR test results and get their anticoagulant dose titrated. Patients were asked to notify the investigator the occurrence of any ADRs. The knowledge of the patients was reassessed using same validated questionnaire when they came for review. All the data were tabulated, analyzed and compared with data from other studies. The collected data were compiled using Microsoft excel and were presented in graphical format using pie charts, histograms etc. Calculation of the mean and standard deviation were done by using statistical calculators. INR evaluation was done and find out the fraction of INRs within therapeutic range. The paired sample t-test was used to compare the patient knowledge score before and after the intervention.

RESULTS

The tables 1-10 below describe the distribution of gender and age, educational status, comorbidities, various indications for oral anticoagulants, recommended target INRs, evaluation of INRs, Adverse effects, drug interactions identified by the anticoagulation clinic.

Patient's baseline knowledge was assessed by means of a validated questionnaire of 21 questions and the mean score was found to be 3.6 ± 5.55 . All the patients were provided counseling by a clinical pharmacist and an information booklet on oral anticoagulation. The patient's knowledge on oral anticoagulation was reassessed using the same questionnaire when they came for follow up (after 2-3 weeks). A mean score of 17.0 ± 2.20 was obtained after the intervention. The paired sample t-test was used to compare the patient knowledge score before and after the intervention. Figure 1 depicts the knowledge assessment score before and after educational intervention of stroke patients who are on oral anticoagulants

29 adverse reactions were observed out of which 8 were major. It includes intracranial hemorrhage, intraperitoneal hemorrhage and drop in haemoglobin concentration requiring blood transfusion. Hematoma was an adverse drug reaction observed due to the use of parenteral anticoagulant heparin. The table 9 below shows the ADRs reported during the study in the stroke department.

10 interactions with oral anticoagulants were observed which is shown in the table 10. These interactions were resolved by the anticoagulation service team. Out of which 1 was drug-food interaction.

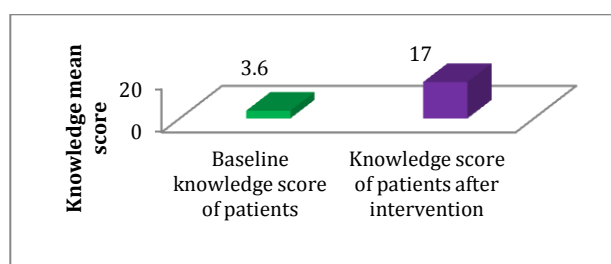


Figure1: Knowledge assessment score before and after educational intervention of stroke patients

Table 1: Gender distribution of patients in stroke department

Gender	Number of patients	% of patients
Male	27	62.8
Female	16	37.2
Total	43	100

Table 2: Age distribution of patients in the study sample (n=43)

Age group	Number of patients	% of patients
< 40 Years	6	14.0
40 - 49 Years	11	25.6
50 - 59 Years	12	27.9
60 - 69 Years.	11	25.6
≥70	3	7.0
Total	43	100

Table 3: Educational status of stroke patients in the study sample (n=43)

Educational status	Number of patients	% of patients
Mid School	5	11.6
High School	6	14.0
Higher Secondary	6	14.0
Graduate	13	30.2
Post Graduate	3	7.0
Diploma	3	7.0
Professional	7	16.3
Total	43	100

Table 4: Comorbidities of the study patients from the stroke department (n=43)

Co morbidities	No.(%) of patients
DM- Diabetes Mellitus	19 (44.1%)
HTN-hypertension	22 (51.1%)
Asthma	5 (11.6%)
Dyslipidemia	21 (48.8%)
Acute Bronchitis	1 (2.3%)
Gastro Intestinal Ulcer	1 (2.3%)
Seizures	6 (13.9%)
RHD- Rheumatic heart disease/CAD-coronary artery disease	9 (20.9%)
Depression	3 (6.9%)
CHF- Congestive heart failure	2 (4.6%)
Psoriasis	1 (2.3%)
Systemic lupus erythematosus	1 (2.3%)
Psoriatic arthritis	1 (2.3%)
Chronic Obstructive Pulmonary Disorder	2 (4.6%)
Total	100%

Table 5: Indications of anticoagulation in stroke patients (n=43)

Indications	No. (%) of Patients
Atrial Fibrillation (AF)	15 (34.88%)
Atrial Fibrillation with valvotomy	1 (2.32%)
Double valve replacement	3 (6.97%)
Double valve replacement with AF	1 (2.32%)
Mitral valve replacement	4 (9.3%)
Mitral valve replacement with AF	1 (2.32%)
Deep vein thrombosis (DVT)	2 (4.65%)
Pulmonary embolism (PE)	2 (4.65%)
DVT with PE	2 (4.65%)
Cortical vein thrombosis (VTE)	1 (2.32%)
Myocardial infarction (MI)	3 (6.97%)
Secondary prevention of stroke	3 (6.97%)
Patent foramen ovale (PFO)	5 (11.6%)
Total	100%

Table 6: Indications and target INR recommended for the study patients in stroke department (n=43)

Indications	Target INR	Number of patients	% of patients
Secondary prevention of stroke, Double valve replacement(DVR)	2.0-2.5	6	14.0
Atrial fibrillation(AF), PFO, DVT, PE	2.0-3.0	29	67.4
MVR with AF	2.5-3.0	1	2.3
MVR, DVR	2.5-3.5	5	11.6
MVR, DVR	3.0-3.5	2	4.7
Total		43	100

Table 7: Evaluation of INR Results in stroke patients

INR results	Values
Total INR checks	782
INRs within target range [No. (%)]	450 (57.5)
INRs > target range [No. (%)]	133 (17.0)
INRs < target range [No. (%)]	199 (25.4)
INRs > 5 [No. (%)]	12 (1.5)
INRs >8 [No. (%)]	4 (0.5)
INRs < 1 [No. (%)]	121 (15.5)

Table 8: Fraction of INRs within therapeutic range for the study patients in the stroke department (n=43)

INR details	Values
Total no. of INRs checked	782
No of INRs within the target range	450
Fraction of INRs within therapeutic range	0.575

Table 9: Adverse drug reactions observed in stroke patients on anticoagulation (n=43)

ADRs	Number
Intracranial Hemorrhage	5
Intraperitoneal Hemorrhage	1
drop in Hemoglobin- transfusion needed	2
Nose bleed	3
Gum bleed	5
Haemetemesis	1
GI disturbances	3
Rash	3
Alopecia	2
Increased LFTs	1
Heavy menstrual bleed	2
Hematoma	1
Total	29

Table 10: Drug and food interactions observed in study group (n=43)

Interacting agents	Interaction	Number of occurrence
Fluoxetine	Increased anticoagulation effect	2
Alcohol	Increased anticoagulation effect	1
Antifungal cream (Fourderm®)	Decreased anticoagulation effect	1
Atorvastatin	Decreased anticoagulation effect	1
Phenytoin	Decreased anticoagulation effect	1
Drug interactions	Increased anticoagulation effect	1
Ampicillin	Increased anticoagulation effect	1
Amitypylline	Increased anticoagulation effect	1
Food interactions	Increased anticoagulation effect	1
Sulfasalazine	Increased anticoagulation effect	1
Green vegetables	Decreased anticoagulation effect	1
Total		10

STATISTICAL ANALYSIS

The paired sample t-test was used to compare the patient knowledge score before and after the intervention. Table 11 shows the paired sample t-test.

A p value of < 0.05 is considered significant. A p value of 0.000 indicates significant improvement in knowledge after patient education.

Hence patient's knowledge on oral anticoagulation improved after counseling by a clinical pharmacist in anticoagulation clinic. The

clinical outcomes measured by the clinical pharmacist in the anticoagulation service were shown in the table 12.

Table 11: Paired sample t-test.

Stroke patients	Difference of the means	t - value	df	p - value
	-13.395	-17.549	42	0.000

Table 12: Clinical outcomes of stroke patients on oral anticoagulants during the study period

Parameters	Values
Number of patients audited	43
Total number of INRs checked	782
Fraction of INRs within therapeutic range	0.575
% of patients with INR > 5	1.5
% of patients with INR > 8	0.5
% of patients with INR < 1 unit from target INR	15.5
% of patients suffering from major bleed in first month of therapy whose INR is above the therapeutic range	2.3
% of patients suffering from major bleed in first month of therapy at any INR	4.6
Average time for each patient to reach therapeutic INR	11.76 days
% of patients who achieve the target INR after 10 weeks	2.3
% of patients who lost to follow up	2.3
% of patients received interacting drugs	25.5
% of patients with adverse drug reactions	41.8
% of patient over due for lab test (i.e., not checked INR).	6.9
% of patients who are unaware of their diagnosis.	Nil
% of patients without proper education.	Nil
% of patients without written documented diagnosis.	Nil

DISCUSSION

Anticoagulation management is a challenging task for healthcare professionals especially for clinical pharmacists. It is 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. Proper educational guidance and monitoring of the INR status regularly and proper dose titrations is the only step for the successful anticoagulation. Several other studies^{2,7,8,9,10} have showed the effectiveness of clinical pharmacists in outpatient and inpatient anticoagulation management. Anticoagulation management service is to monitor and adjust one's anticoagulation medications for the period of time they need to be on anticoagulation therapy. They are run mostly by pharmacists and help in assisting physicians. Anticoagulation clinics are therefore recommended for the hospitals to manage and coordinate such services.

The study results of the stroke department demonstrate that the patients were within their desired INR range more significantly. The supportive ambience from the physicians and other staff in the department helped in better anticoagulation for the patients and experienced only a few thromboembolic events. The study results of the stroke department demonstrate that the patients were within their desired INR range more significantly. The supportive ambience from the physicians and other staff in the department helped in better anticoagulation for the patients and experienced only a few thromboembolic events. All 47 patients admitted to the stroke department during the study period were selected, but only 43 could complete the study. 3 of the patients had expired (one was an APLA patient with cardiac issues, other one was age related death while third one had congenital heart disorders) and one patient was lost to follow up. Out of 782 total INR checks of 43 audited patients about 57.5% were within target range which showed similar results to the of study carried by *Nadia A Amruso*⁴. The fraction of INRs within therapeutic range was 0.575 for the present study.

The patients were interviewed during their stay in hospital and during their follow up in the OP after discharge. The demographic details, social and medical history were collected and initial knowledge regarding anticoagulation was assessed. Oral anticoagulation knowledge was assessed by a validated questionnaire. Counseling regarding oral anticoagulants was given to patient and / their caregivers and were also provided with patient information booklets. The doubts were cleared throughout their stay in the hospital. Contact number of the anticoagulation service was given to patients and caregivers on discharge to report INR results, get their dose titrated and for clarification of any doubts regarding anticoagulation. During the follow up, the knowledge on anticoagulation was reassessed and the average score of patient knowledge assessment score increased to 17.0 ± 2.20 from 3.6 ± 5.55 after counseling. The Paired 't' test indicated that there was statistically significant difference in the scores ($p < 0.05$) and it is evident that the clinical pharmacist's intervention improved the patient's knowledge on oral anticoagulation. A good communication and contact was maintained with the patients by the clinical pharmacist who helped the patients to clarify their doubts and discuss the matters regarding anticoagulation therapy and it was difficult for them to reach the physicians directly. Better levels of the knowledge of the patients may also be achieved if the information is reinforced by simple measures such as repetition of knowledge assessing questionnaires to make patients/ caregivers answer it or use of written materials like leaflets/booklets. The availability of a non-physician counselor such as a clinical pharmacist has shown to increase the patient's knowledge about their health and disease condition, treatment undertaken/required, medications, importance of adhering to therapy etc.¹¹

The anticoagulation service was able to educate well the patients about anticoagulation, to bring the INRs of patient into target range by proper and timely dose titrations, to identify adverse drug reactions, drug drug interactions and drug food interactions and bring about proper interventions. Poor doctor-patient communication can be overcome by the involvement of a clinical pharmacist. Moreover they can act as good communicators between physicians and patients. More effective communication arises from understanding the patient's expectations, involving the patients in negotiating their treatment plan and the continuity and accessibility of the staff¹². The study also had an aim to prove the necessity to establish anticoagulation services for the benefit of the patients and clinicians in the hospital departments where there are patients on anticoagulation. Oncall phone was provided for the clinical pharmacist to follow up patients and help in dose titration of oral anticoagulants based on INR results. The patients had good cooperation and contact with the service. Telephonic management of the INR and resolving other issues regarding anticoagulation therapy was found to be better through the anticoagulation service. Patients were satisfied with the telephonic based anticoagulation management. And about 100% satisfaction was reported in the present study. Similar studies^{13, 14} also support the fact of better anticoagulation management by the clinical pharmacist through telephonic means. Most patients received helpful information from an anticoagulation service and the convenience, accessibility, and services provided by anticoagulation service personnel were "better than expected". This was assessed by making patients/ caregivers answering a set of satisfaction assessment questionnaires. The doctors and other medical staffs were also satisfied in the anticoagulation service by clinical pharmacist. The study results reflect the impact of a clinical pharmacist on anticoagulation management and the need for anticoagulation services in the hospital settings.

CONCLUSION

The establishment of anticoagulation clinic in the hospital helped the Stroke unit in bringing their patients under targeted anticoagulation. It helped in improving patient's knowledge compliance, reducing incidence of interactions and adverse effects. Thus clinic laid a foundation in building good and healthy relation between physician, pharmacist and patients. Since a clinical pharmacist can efficiently manage anticoagulation and provide optimal care, it is recommended that major hospitals both in government and

corporate sector should consider providing clinical pharmacist managed anticoagulation service/ clinic for the benefits of patients.

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