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Safety and Efficacy of Newer Oral Anticoagulants in Coronary Artery Disease Patients: A Prospective Observational Study

Murali Krishna Kandukuri [1], Dr. K. Karthickeyan[2]

[1]Research Scholar, School of Pharmaceutical Sciences,Vels Institute of Science, Technology and Advanced Studies (VISTAS),Pallavaram, Chennai–600117, Tamil Nadu, India

Email ID : muralikrishna.kandukuri3@gmail.com

[2]Professor and Head, PhD Guide,Department of Pharmacy Practice,School of Pharmaceutical Sciences,Vels Institute of Science, Technology and Advanced Studies (VISTAS),Pallavaram, Chennai–600117, Tamil Nadu, India

Email ID: hodppractice@velsuniv.ac.in

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ABSTRACT

Background: Coronary artery disease (CAD) is a major contributor to morbidity and mortality globally. Anticoagulation plays a pivotal role in managing thromboembolic complications. While traditional anticoagulants like warfarin and heparin are widely used, they are associated with limitations including bleeding risks and intensive monitoring. Newer oral anticoagulants (NOACs) such as apixaban and dabigatran offer a promising alternative.
Objective: To prospectively evaluate and compare the safety and adverse effect profile of newer oral anticoagulants (apixaban, dabigatran) with traditional agents (warfarin, heparin) in CAD patients under real-world clinical conditions.
Methods: A 12-month, open-label, parallel-group, observational study was conducted at Vijaya Hospital, Nellore. A total of 200 patients aged 30–60 with diagnosed CAD were included—100 on NOACs and 100 on older agents. Adverse drug reactions (ADRs) were evaluated using a structured questionnaire (CADSEQ), patient diaries, and WHO-UMC causality assessment.
Results: NOACs exhibited significantly fewer adverse events (13%) compared to warfarin/heparin (42%). Major bleeding, liver dysfunction, and hypersensitivity reactions were markedly lower in the NOAC group ($p< 0.05$). Patient adherence and satisfaction were improved with NOACs due to ease of administration and reduced monitoring needs.
Conclusion: NOACs demonstrate superior safety, tolerability, and compliance in CAD management. Their role should be expanded, especially in high-risk or poorly monitored populations. Further studies in special populations such as neonates or pediatric CAD cases may help shape safe usage protocols.

Keywords: *Apixaban, Dabigatran, Warfarin, Anticoagulants, Coronary artery disease, Safety, Real-world evidence.*

1. INTRODUCTION

Coronary artery disease (CAD) represents the primary cause of cardiovascular mortality worldwide. The pathogenesis involves atherosclerosis, endothelial dysfunction, and thrombosis, necessitating chronic antithrombotic therapy. Traditional anticoagulants like warfarin and heparin, though effective, come with drawbacks including dietary interactions, narrow therapeutic windows, and the need for frequent INR monitoring. Newer oral anticoagulants (NOACs)—such as apixaban and dabigatran—offer fixed dosing, reduced monitoring requirements, and better safety profiles.This study aims to assess the real-world safety and adverse event profiles of NOACs in CAD patients and to compare these outcomes against those seen with traditional agents.

Materials and Methods

This study was designed as a prospective, open-label, comparative observational study conducted over a duration of 12 months at Vijaya Hospital, Nellore, Andhra Pradesh. A total of 200 patients diagnosed with coronary artery disease (CAD) were enrolled, with 100 patients receiving newer oral anticoagulants (NOACs), specifically apixaban or dabigatran, and the remaining 100 patients receiving traditional anticoagulants, namely warfarin or heparin.

Inclusion and Exclusion Criteria

The inclusion criteria comprised patients aged between 30 and 60 years with a confirmed diagnosis of CAD and a current prescription for one of the study anticoagulants, provided they gave informed consent. Exclusion criteria included known

hypersensitivity to any study medication, age below 30 years, pregnancy, or any history of adverse reactions to the medications under investigation.

Adverse events were monitored using a locally developed and validated Coronary Artery Disease Side-Effect Questionnaire (CADSEQ), which was also translated into Telugu for better patient understanding. Patients were followed up at 3, 6, 9, and 12 months, during which adverse reactions were recorded and assessed using the WHO-Uppsala Monitoring Centre (WHO-UMC) causality classification system. Data collection involved capturing demographic details, medication histories, physical examination findings, and reviews of patient-maintained diaries at each follow-up visit. Statistical analysis was carried out using the Chi-square test to compare the frequency of adverse events between groups, and a p-value of less than 0.05 was considered statistically .

CAD Side-effects Evaluation Questionnaire (CADSEQ)

To make the inquiry of Coronary artery disease side-effects comprehensive convenient, we developed a new questionnaire by clubbing some items anddeveloped by some of the physicians of cardiology department and compiled the following subject The common questionnares included were in the present study include

Majorbleeding, Gastrointestinal bleeding,retroperitoneal bleeding, Hypersensityvity reactions, Liver damages, Thrombosis after disconnection and increased risk of patients and it

was shown in Table 1

Table : 1 Common Questionnaire

S.NO	Symptoms	Questionnare	Never	Rarely	Often	Always
1	External bleeding (Ecchymosis ,Epistaxis)	Whether you faced any unusal bleeding from the gums, nose bleeds.	0	2	3	1
2.	Gastro intestinal bleeding	Do you observed any blood vomitings, blood stools	0	4	4	2
		Do you observed any color change in urine				
		What is the color of urine and stool	0	1	2	3
3.	Hematuria		0	1	2	3
		Do you feel tired in your work and giddiness				
		Do you feel any discomfort in breathing				
4.		Do you feel any symptoms of asthma	3	2	1	0
	Anemia		3	2	1	0
		Do you find any swelling in the face, lips, tongue	0	1	2	3
5	Hyper sensitivity reactions	Do you face the problem of continuos wheezing	0	1	2	3
		Do you find any rashes on the skin				
6.	Thrombotic events after	Do you observed any numbness in one side of the body	4	3	2	1

	abrupt discontinuation	Do you feel any symptoms of paralysis				
		Do you feel the symptoms of Jaundice	0	1	2	3
			0	0	0	0
		Do you have any discomfort in the chest pain				
7.	Liver Dysfunction		0	0	0	0
		Do you have any discomfort in the Abdominal pain	0	1	2	3
		Do you undergone any liver test for checking liver enzyme	3	2	1	0
		Do you feel decreased out put of urine	0	1	2	3
		Do you feel fatigue conditions	0	1	2	3
		Do you feel severe headache, Confusion state	3	2	1	3
			3	3	3	3
8.			0	1	2	3
9.						
.	Kidney injury					
	Neurological					

This questionnaire was used in the study to collect information on possible side- effects of Newer oral anticoagulants drugs prescribed to the patient including study drug. The questionnaire was translated to Telugu language by a certified translation agency. Translated versions of questionnaire were reviewed by Cardiologist participating in the study for further adaptation to local patient's understandings. Researcher interviewed the patient and/ or care taker using this questionnaire on each physical visit to the site e.g. screening & enrolment (day 1), 6 month visit and 12 month visit. For any clarification as well as for patient cooperation, the first interview was conducted under supervision of treating Coronary artery disease

Patient Diary

Enrolled patients are provided patient diary to record adverse event if experienced any between study visits. The patient/

caregiver are trained on how to fill the diary on enrollment visit. On each visit this patient diary is reviewed for records of adverse events and the records are discussed with treating Cardiologist to confirm adverse events. Whenever patient/ care giver telephonically reports an adverse event, they are instructed to record details of the event in patient diary as well. The patient diary was translated in teluguby professional translating agency for better understanding of patient/ caregiver. At the end of study i.e. 12 month visit, the diary will be collected back from the patient and filed as source document.

Duration of the Study

With the help of treating psychiatrist, patients were followed up at 3 month (±1 month, telephonically), 6 month (±1 month, physically), 9 months (±1 month, telephonically) and 12 months (±1 month, physically) over a period of 1 year and monitored for development of any adverse,effects.

Visit	1	2	3	4	5
Purpose	Screening& Enrollment	Tel	Phys	Tel	Phys
Month	0	3 ± 1	6 ± 1	9 ± 1	12 ± 1
InformedConsent	√				
DemographyRecording	√				
Medical History Recording	√	√	√	√	√
Medication History	√	√	√	√	√
CheckSelection Criteria	√				
ASEQ[1]	√		√		√
PhysicalExamination(+Body Weight)[2]			√		√
CausalityAssessment (WHOUMC criteria)[3]		√	√	√	√
PatientDiaryIssuing&Training	√				
Patient Diary Review			√		√
PatientDiaryCollection					√

Tel–Telephonic,Phys–Physical

Coronary artery disease Side-effect Evaluation Questionnaire (CADSEQ) was used as an interview to inquire patients about development of any adverse events. Any significant change in these questionnaire items was reported to Cardiologists to identify adverse events.During physical visits 3 & 5, in case of suspected adverse events, physical examination including

body weight was performed by / doctor to confirm the Cardiologists AE, if necessary.For all confirmed adverse events, Investigator performed causality assessment based on World Health Organization Uppsala Monitoring Centre (WHO- UMC) criteria.

Visit WiseActivities

ScreeningandEnrollmentVisit(Day0,Month0)

Following activities were undertaken at this visit on patients allocated by the study by treating Cardiologists Obtained written informed consent of the patients with the help of patient information sheet and informed consent form Recorded demographic characteristics (dateofbirth/age,sex,weight etc.Recorded medical history (past & present history of relevant medical disease and plagues) Recorded medication history (details of medication prescribed and ongoing) Inquired and filled up CADSEQ with the help of Cardiologists Checked for selection criteria and enrolled the patient if found eligible Collected contact details of enrolled patient/caregiver Dispensed diary to record adverse events,if experienced any,during the period between visits and trained patient or caregiver/ LAR on filling diary Informed patient or caregiver/ LAR about all study visits including possibility of physical/ telephonic visit and activities involved in the visits

TelephonicFollow-upVisits[EndofMonth3(±1)&9(±1)]

At each of these visits,patient/caregiver were contacted telephonically to collect following information: Adverse events, if experienced any since last visit Medication history (details of medication prescribed since last study visit). If there was discontinuation of the study drug started on visit 1, patient was discontinued from the study If patient was investigated by laboratory or electrocardiography since lastvisit, was asked to convey the important abnormality in the next physical visit If any adverse event is suspected, it was brought to the notice of treating cardiologist at the next physical Informed Patient about subsequent study visit,as applicable.

PhysicalFollow-up Visits [End ofMonth6(±1)&12(±1)]

At each of this follow up visits, following activities were done on patient:

Inquired about adverse events, if experienced any since last visit and reviewed the patient diary, if available, for adverse events Recorded medication history (details of medication prescribed since last study visit)Inquired and filled up CADSEQ to identify development of adverse events. Any significant change in this questionnaire was reported to to identify adverse eventsIn case of suspected adverse event since last visit, treating cardiologistwas requested for physical examination including body weight for confirming the adverse events,if necessary.Any significant change in the findingsofphysical examination or body weight (> 7% from baseline) was discussed with the cardiologistto verify the suspected adverse eventIf any adverse event was suspected since last visit, it was brought to the notice of treating and if confirmed, information on actions taken for the adverse event was collected. For all confirmed adverse events, causality assessment was performed based on WHO-UMC criteria At 6 month visit patient or caregiver was informed about subsequent study visit and at 12 month visit, patient or caregiver was informed about end of the study Additionally, throughout the study, if patient reports any adverse experience between the study visits, it was recorded and communicated to treating cardiologist to identify adverse event, if any, during subsequent visit and assist treating cardiologist to undertake necessary actions, as applicable to relieve or reduce the adverse event.

Data Collection

Following Source Documentation and Case Report Form(CRF) Entries were made

Records of demography,relevant medical history,medication history,physical examination

findings(includingbodyweight)were documented insource data and relevant details were transcribed to CRF Relevant investigation results, when available were transcribed to CRF.Filled ADSEQ were maintained as source documents and its scores were transcribed to CRF.For all adverse events identified in the study, adverse event form in the CRF was filled up.Causality assessment was performed as per WHO-UMC criteria and was documented in adverse event form in the CRF.At the end of study, adverse event database was prepared from the relevant data captured in CRFs of all enrolled patients and analyzed for the study end points.

The comparison of adverse events between newer oral anti coagulant and traditional anticoagulants group were shown in table 3 and for easy understanding it is represented as bar diagram and pie charts (Shows adverse events of NOAC”S) which was shown in fig 1 and fig

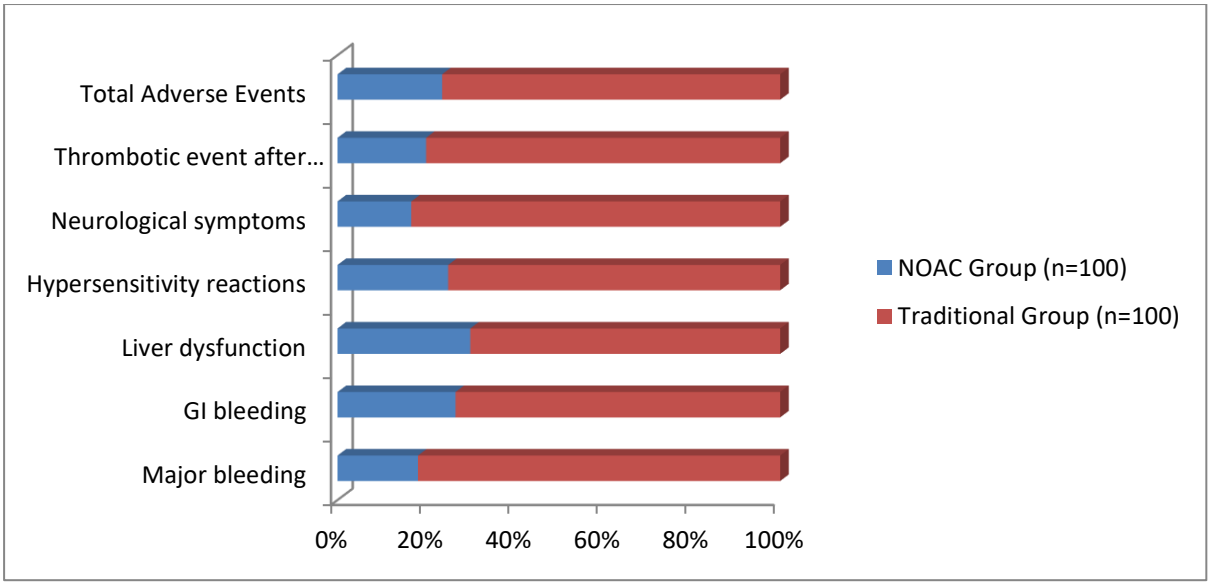

Figure 1: Bar Chart Showing Comparison of Adverse Events

Table 3: Comparison of Adverse Events between NOAC and Traditional Anticoagulant Groups

2. RESULTS

Adverse Event	NOAC Group (n=100)	Traditional Group (n=100)
Major bleeding	2	9
GI bleeding	4	11
Liver dysfunction	3	7
Hypersensitivity reactions	2	6
Neurological symptoms	1	5
Thrombotic event post-discontinuation	1	4
Total adverse events	13	42

Patients on NOACs had significantly fewer adverse events ($p < 0.05$)

Better adherence due to less monitoring and fixed dosing

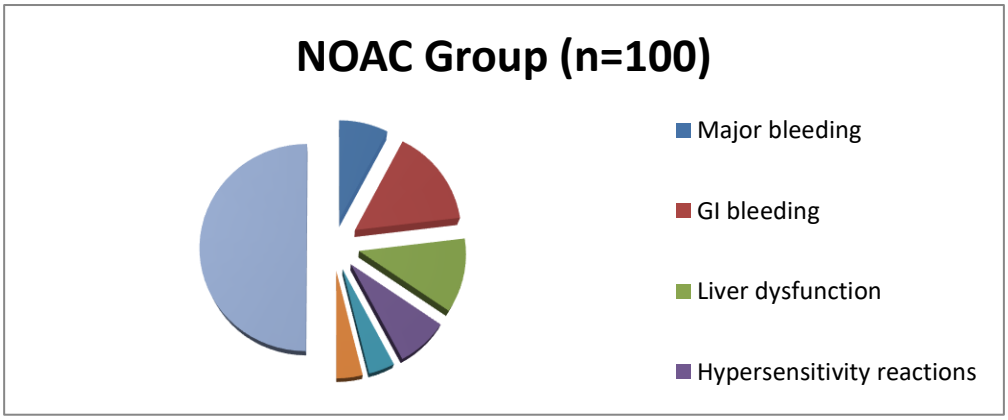

Figure 2: Pie Chart Showing different Adverse Events of Newer oral anticoagulnts

3. DISCUSSION

This real-world study affirms that newer oral anticoagulants are safer and more effective alternatives to warfarin and heparin in CAD patients. Their use reduces adverse events and enhances patient convenience. These findings are consistent with global literature, such as the ARISTOTLE and RE-LY trials.

Given the growing relevance of oral anticoagulants in vulnerable populations—including the elderly, patients with comorbidities, and possibly neonates—rigorous long-term studies across all age groups are warranted.

4. CONCLUSION

Newer oral anticoagulants like apixaban and dabigatran provide enhanced safety, reduced bleeding risk, and better patient compliance compared to warfarin and heparin in CAD patients. Their integration into routine CAD management can improve outcomes, especially where monitoring resources are limited.

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Conflict of Interest

The authors declare no conflict of interest.

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