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EFFECT OF PHARMACIST-PROVIDED HEALTH LITERACY FOR PATIENTS ON ORAL ANTICOAGULATION THERAPY

JOJU SEBASTIAN C.*, ALAN KURIAN, LISSA K. SUNNY, PRUDENCE A. RODRIGUES

Department of Pharmacy Practice, PSG College of Pharmacy, Coimbatore, Tamil Nadu India.

***Corresponding Author: Dr. Joju Sebastian C.**
Department of Pharmacy Practice, PSG College of Pharmacy, Coimbatore, Tamil Nadu India.

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ABSTRACT
Oral anticoagulation (OAC) therapy using vitamin K antagonists is commonly used therapy for the prevention and treatment of various thromboembolic complications. It mainly aims to maintain the levels of anticoagulation capable of preventing thromboembolic events without increasing the risk of hemorrhagic complications. The main reason for the failure of the therapy is the unawareness of the patient regarding the medication. This study is thereby performed to assess the effect of pharmacist-provided health literacy through counseling and information booklet and the improvements in the knowledge and life style of the patient.

OBJECTIVES

- To develop and implement Oral anticoagulation booklet in the Cardiology department.
- To assess the knowledge of OAC therapy among patients.
- Identifying reasons for non-adherence to medication.
- To detect drug related problems.

Method: A total of 86 patients were studied which was divided randomly to control (55) and intervention(31) groups. Both groups were assessed for their knowledge using a questionnaire before and after the counseling to assess the knowledge gained. The patients in the intervention group were discharged with a booklet and both the groups were assessed for the knowledge retained after a period of time by the same questionnaire. **Results:** The study results showed that the patients gained knowledge after counseling and 14% more improvement of knowledge retention in intervention group (62%) than the control group. **Conclusion**: It is possible to conclude that the patients who had been educated by the pharmacist shown improvement in knowledge regarding the therapy. The intervention group who had been given 'patient information booklet' had shown significant improvement in knowledge retention than the control group.

KEYWORDS: Oral anti-coagulation, patient information booklet.

INTRODUCTION
Oral anticoagulation therapy with vitamin K antagonists is the commonly used treatment for the prevention and treatment of various thromboembolic complications viz. atrial fibrillation, deep vein thrombosis, pulmonary embolism, heart valve diseases and prosthetic valve replacement. It mainly aims to maintain the levels of anti-coagulation capable of preventing thromboembolic events without increasing the risk of hemorrhagic complications.[1,2]

Vitamin K is critical to the conversion of certain glutamate residues to gamma-carboxy-glutamate residues in clotting factors, VII, IX, X and XI. Vitamin K antagonists block the reduction of oxidized vitamin K leading to its deficiency causing reduced production of clotting factors.[1,2]

The treatment being a complex work up, needs monitoring which is carried out by PT-INR test for which the recommended values are between 2-3 and 2.5-3.5(for valve replacement cases).[3] PT-INR value above 3.5 and below 2 leads to super therapeutic and sub therapeutic (treatment failure) complications respectively (Table 1).[4] These complications may arise based on factors like drug-drug interactions (Table 2a,2b)[3] and Drug-food interactions (Table 3)[5] which are most neglected factors once the patient go back home, after discharge from hospital.

Table 1: Complications of anticoagulation therapy.

Super Therapeutic Complications (INR>3)	Sub Therapeutic Complications (INR<2)
Major complications	
Prolonged bleeding from cuts and wounds	Stroke
Malena	Deep vein thrombosis
Rashes	Pulmonary embolism
Hematuria	Myocardial infarction
Increased menstrual bleeding	Peripheral arterial disease
Intra cranial haemorrhage	
Minor complications	
Gum bleed	
Nose bleed	
Easy bruising	

Table 2a: Drug interactions with Warfarin/Acitrom-Mechanism.

Increased accumulation of acitrom Inhibition of the metabolic enzyme CYP2C9, causing reduced clearance leading to accumulation.	**Reduced availability of acitrom** Induction of CYP2C9, causing increased clearance.
Altered level of vitamin K Alteration of intestinal bacterial flora causes disturbance in absorption of vitamin K causing fluctuations in vitamin K levels.	**Displacement of anticoagulant from plasma albumin** Warfarin is bound with albumin in plasma. Drug displaces warfarin from albumin, increases warfarin circulation, causing bleeding.

Table 2b: Drugs interacting with Warfarin/Acitrom.

Some Major Drug Interactions with Warfarin/Acitrom		
INCREASED Effect of Warfarin		**DECREASED Effect of Warfarin**
Anti-Platelet Agents: Abciximab, Aspirin, Dipyridamole, NSAIDs, Clopidogrel, Tirofiban	Analgesics: Paracetamol (Large Doses ie. 4 to 7g Per Week), Tramadol	Ascorbic Acid (Large Doses) Vitamin K
COX-2 Inhibitors: Celecoxib, Rofecoxib	Anticonvulsants : Phenytoin	Anticonvulsants**:** Carbamazepine, Phenytoin
Antibiotics: Cephalosporins, Macrolides, Metronidazole, Sulphonamides, Quinolones, Vancomycin	Selective Serotonin Reuptake Inhibitors: Fluoxetine	Antibiotics: Rifampicin, Rifabutin
Antifungals: Itraconazole, Fluconazole, Ketoconazole	Tricyclic Antidepressants	Sedatives: Barbiturates
Antiarrythmics: Amiodarone, Mexiletine, Verapamil	Raloxifene, Tamoxifen	
Herbal Medicines: Garlic, Papaya, St Johns Wort, Ginkgo, Ginger and Garlic (Large Amounts), Guarana.	Quinine and Quinidine	Herbal Medicines: Ginseng, Slippery Elm Bark, Green Tea, Co-Enzyme Q10

Table 3: Foods classified as per the content of Vitamin K which interacts with Warfarin/ Acitrom.

Food with low Vit K	Foods with moderate vit K	Foods with high vit K
Carrot	Red cabbage	Broccoli
	Green peas	Cabbage (raw)
Corn, potato	Pickle,Dill(*sada kuppi*)	Lettuce
eads, cereals	Margarine (veg butter)	Spinach (cooked and raw)
Rice	Olive oil	Mayonnaise
Fruit and juices		Liver
Milk ,cheese		Soybean oil
Eggs and butter		Broccoli (cooked)
Sunflower oil, sesame oil		Green beans, cauliflower
Fish, meat, pork, chicken.		
Table 3: Foods classified according to level of Vit K which interact with Warfarin/ Acitrom		

In a study on drug related hospital admissions in a tertiary care hospital in south India, anticoagulants were responsible for 9.9% of cases of drug related hospital admissions.[6] The study was conducted with a hypothesis whether educating patient with relevant information regarding drug-use, importance of monitoring and diet may have an influential role in minimizing drug related issues due to acenocoumarol/warfarin.

AIM AND OBJECTIVES

To enhance and evaluate patient's knowledge and adherence to oral anticoagulation therapy by pharmacist-provided health education.

The objectives of the study are the following:

- To develop and implement oral anticoagulation patient information booklet in cardiology ward.
- To provide and assess the knowledge regarding the therapy in the target patients.
- To identify the reasons for the non-adherance of medication.
- To detect, report and minimize drug related issues during and after the hospital stay.

MATERIALS AND METHODS

Study Design: Prospective interventional comparative study.

Study Population: In-patients and out-patients getting admitted under cardiology and CTVS departments in PSG Hospitals who are prescribed with the oral anticoagulant drug, Acenocoumarol/Warfarin.

Study Duration: February to July 2014(6 months).

Study Site: This prospective – observational comparative study was conducted at the teaching hospital of PSG Medical Sciences and Research Institute, Coimbatore. This is a multispecialty 1400 bedded tertiary care hospital located in the south region of Tamil Nadu.

Randomization: Patients on acenocoumarol were randomized into two groups. Usual care group is provided with counselling and intervention group is given counselling along with OAC booklet.

Inclusion Criteria

• In-patients/out-patients who are on oral anticoagulation therapy with Acitrom/ Warf.

• Patients (or with by-stander) who can both read and write either Tamil or English.

Exclusion Criteria

- Deafness
- Visual impairment.

Statistical Analysis

- Mann Whitney U test
- Paired t-Test.

Sample size: 50 patients in each arm (totally 100 patients).

Study tools

- Oral anti-coagulation knowledge assessment questionnaire (herein after termed as OAC-KAQ).[7]
- MORISKY 8 item medication adherence scale.
- OAC therapy patient information booklet (as counselling aid).

Outcome Measures

- Knowledge retention.
- Medication adherence.
- Adverse drug events.
- INR control (during hospital stay and review).

Study Procedure

Signed Informed consent received from those patients who were administered with Acitrom after getting approval from the institutional ethics committee.

Phase 1: This was carried out in the first 55 volunteers. Their knowledge regarding the therapy was assessed, counselling was given regarding the therapy and post counselling knowledge was assessed. This was done using OAC-Knowledge Assessment Questionnaire (KAQ).[7]

Data consolidation for the preparation of the booklet was done.

Phase 2: ACITROM/WARF patient information booklet was prepared and it was reviewed and implemented by cardiology physician. Data collection, counselling and knowledge assessment (OAC-KAQ) was performed on an intervention group of 31 volunteers. On discharge the patients were provided with the patient information booklet. **Phase 3:** Follow up of patients conducted when they came for review or via telephone interview. Knowledge assessment (using OAC-KAQ) and medication adherence (MORISKY 8 item questionnaire) was carried out during the follow up. Drug, lifestyle and diet related doubts of patients were cleared after thorough reference and professional suggestions.

Statistical Analysis

- Performed using Graph pad PRISM version 5.03.
- Paired t test - to compare the mean health literacy before and after providing counseling to patients.
- Mann Whitney U test – To compare the knowledge retention in patients of the control and intervention group.
- P value < 0.05 was considered as significant.

RESULTS

Flow Chart of Events

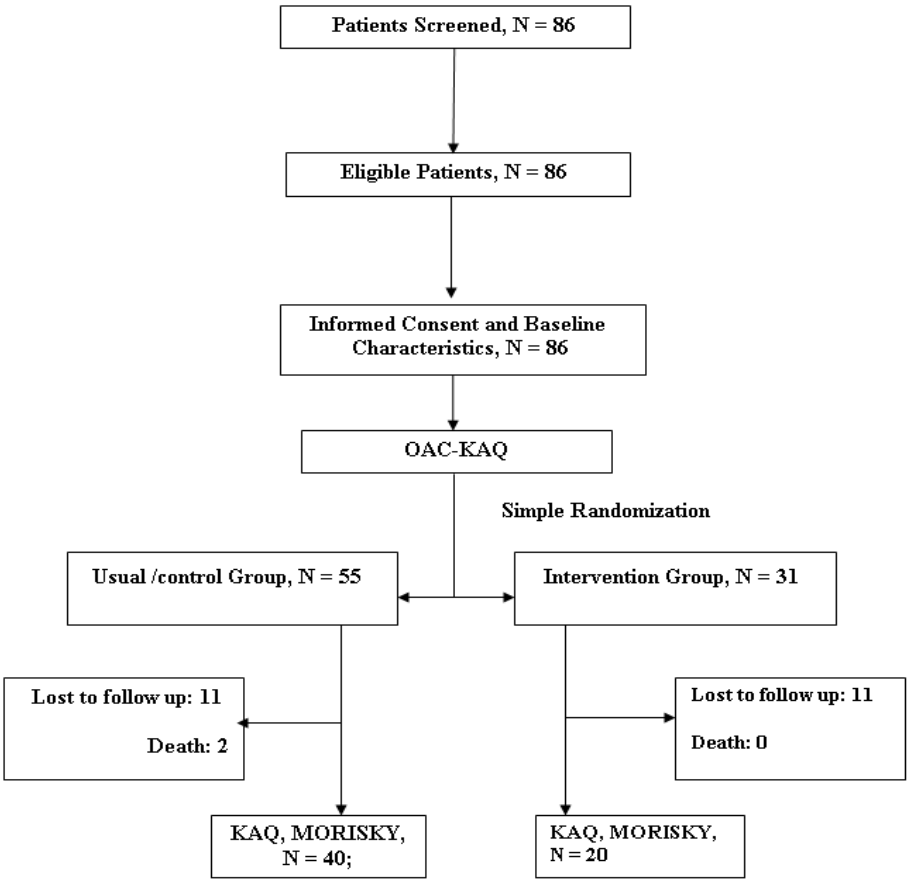

Fig. 2: Flow of Events.

Total of 86 volunteers were recruited for the study. A total of 55 were recruited as control group and 31 patients as the intervention group.

In the study 38 (44%) patients were recruited from CTVS department and 48 (56%) patients from the Cardiology department. Among this 43% (37) were female and 57% (49) males.

Maximum number of subjects included in the study was people in the age group of 20-39 (35%), 40-59 (35%), 60-79 (29%) and 0-19 (1%).

The primary language mostly used for counselling was Tamil (94%). Very few subjects preferred English (4%) and Malayalam (2%).

Social habits monitored were cigarette smoking and alcohol consumption. Most of the subjects were non-smokers (67%) and non- alcoholics (74%).

Acitrom was given to patients with various diagnoses out of which RHD (26%) and AF (19%) were the main diagnosis.

While studying the patients' medical records, they were identified to be having a range of comorbidities. Systemic hypertension (21%), diabetes mellitus (18%) and dyslipidaemia (13%) were encountered more.

Statistical Analysis of Data

Significance of Knowledge Retained In Between Control Group And Intervention Group:

Knowledge regarding Acitrom therapy which was provided during hospital stay was checked for assessing the knowledge retained during review/ telephone interview. The intervention group was found to have more knowledge retained than the control group (Fig. 3).

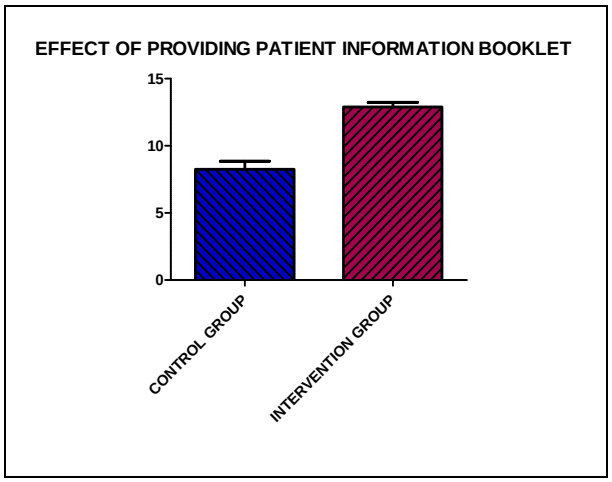

Fig. 3: Effect of Providing Patient Information Booklet (Knowledge Retention Between Control And Intervention).

On segregating the questionnaire into three parts namely, "Drug information" (Fig. 4), "Monitoring information"(Fig. 5) and "Diet and Lifestyle"(Fig. 6), though the intervention group shows significant retention knowledge, retention of Drug Information was found to be significant ($p<0.05$):

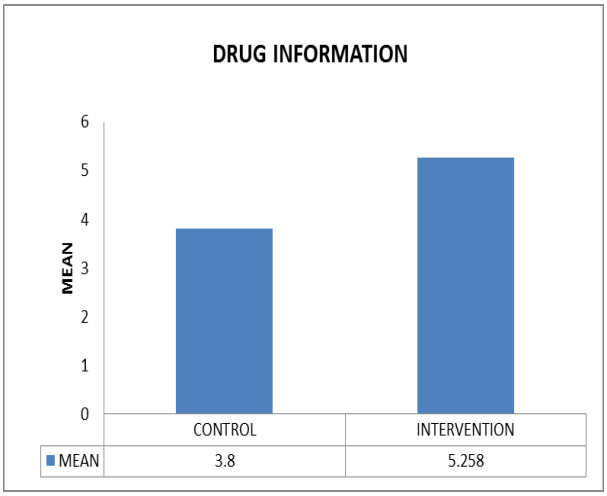

Fig. 4: Drug Information Retained.

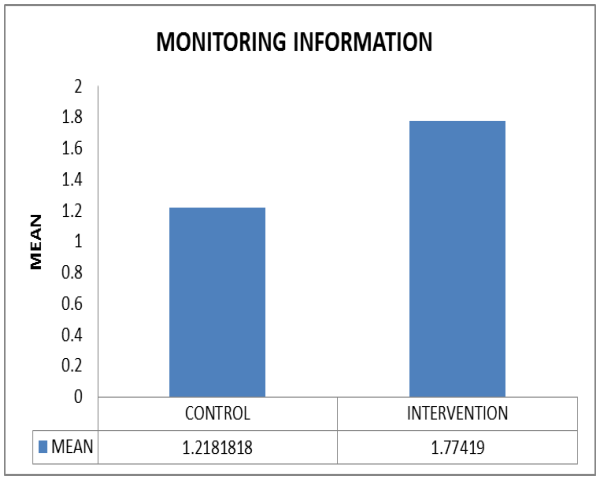

Fig. 5: Monitoring Information retained.

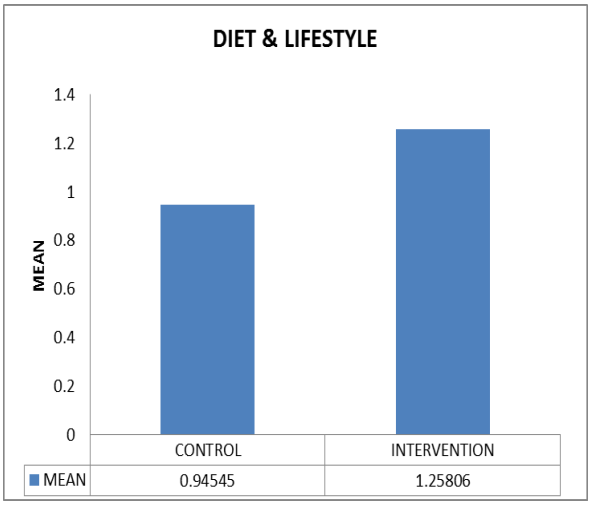

Fig. 6: Diet and Lifestyle information retained.

An overall assessment of knowledge shows a significant retention of drug information than other information provided: Drug information (64%), Monitoring information(21%) and Diet information(15%).

Comparing the difference of knowledge retained between intervention and control, intervention group shows very less decline in knowledge (4%) than the control (22%).

On comparing the knowledge retained between male and female, both shows a significant difference between control and intervention groups. Female group ($p= 0.0005$) is found to be more significant than male ($p= 0.0017$).

People of different age groups were compared based on their knowledge retention level. The intervention group was observed to have retained significant knowledge than the control group in all age groups. The main point to note was that the response from the intervention group (mean= 12.75) was double than that of the control group (mean= 6) of elder age.[60-79]

Significance of Knowledge Imaparted To Patients Through Pharmacist-Provided Health Education

The effect of counselling provided to patients was assessed using OAC-KAQ, before and after counselling. The knowledge difference observed between both the groups was significant ($p<0.0001$)(Fig. 7a & 7b).

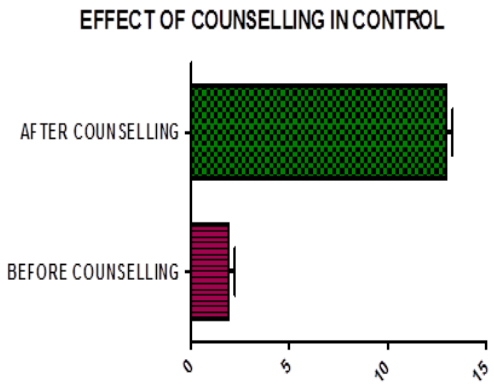

Fig. 7a: Effect of Counselling In The Control Group.

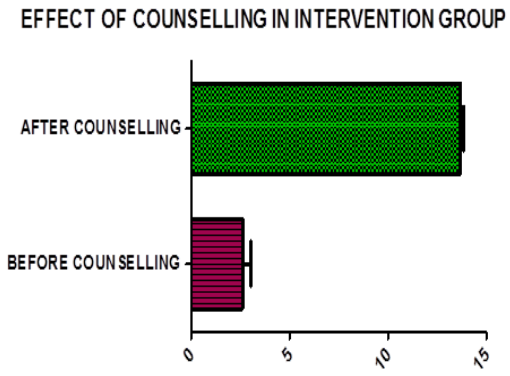

Fig. 7b: Effect of counselling in the intervention group.

Comparing the Knowledge Gained Due To Counselling In Control And Intervention Groups

Knowledge gained via counselling in control group: before couselling-13%, after counselling-87%. Knowledge gained via counselling in the intervention group: before counselling-16%, and after counselling-84%.

Reasons for Non-Adherance As Per Patient's Point Of View

- Myths regarding taking of the missed dose.
- Difficulty in following the same timing of administration (6 PM).
- Difficulty in remembering to take the dose during work and journey.
- Misunderstanding regarding diet.
- Difficulty in following dietary instruction
- Administering both allopathic and alternative medicine (ayurvedic, siddha and unani medicines).

Adverse Drug Events Encountered During The Study

Table 4: Census of ADR Reported.

ADRs	No. Of Cases
Thrombophlebitis / haematoma	1
Haematuria	4
Gum bleed	6
Bruising	4
Intracranial haemorrhage	1
Blood in Sputum	3
Bleeding from surgery site	1
Epistaxis	4
Malena	3
GI discomfort	3
Heavy Menstrual blood flow	3

Drug Interactions Observed

- **Warfarin and Amiodarone** interaction
- A female subject got readmitted as her INR shoot-up to 19 as she was prescribed with Amiodarone and warfarin during the previous discharge.
- On reporting interaction, it got rejected as no dosage adjustment or alternative is possible as per her current condition (Severe AF).

DISCUSSION

The study was conducted in 55 control subjects and 31 intervention subjects. The effect of counselling was observed to be significant in both groups when knowledge assessment was carried out.

There was great demand/request from the control group for a hard copy of the counseling conducted especially at time of discharge.

A similar report was encountered during the literature review, in a study conducted by Deirdre A. Lane; Jennie Ponsford et. al. for The West Birmingham Atrial Fibrillation Project[8], in which it demonstrates the effect of providing a patient information booklet on AF and its OAC therapy- improving the knowledge perception of the people.[13]

Gender wise comparison of knowledge retention found that female had significant knowledge retained than male.

Age-group wise comparison revealed that the intervention doubled the amount of knowledge retained in elderly subjects. Similar result was observed in a study carried out by Tayyaba Irfan Khan et al., 2004, to assess the value of education and self-monitoring in older patients on warfarin therapy- showed improvement of anticoagulation control in elderly patients.[9,14]

On comparing the type of knowledge retained knowledge retained revealed a significant retention of Drug information knowledge. Information retained regarding diet and lifestyle and monitoring information was not significant, but was comparatively higher in the intervention group.

In an analysis study by Angela Coulter and Jo Ellins, 'Effectiveness of strategies of informing, educating and involving patients', which concluded that health information materials, decision aids, self-management action plans and other technologies of patient engagement are most effective when they supplement or augment, rather than replace, interaction between patients and professionals.[10]

In another study, 'Evaluation of patients' knowledge about anticoagulation therapy' by Fiona C. Taylor, says that use of written education guides successfully alert patients to the possible risk and complications of treatment and recommends that guides including posters and leaflets have been instructive in other conditions and promote positive changes in patient's wellbeing and improve compliance.[11]

In the study 'Relationship between patients' warfarin knowledge and anticoagulation control' by Elaine et al., demonstrated that a brief educational intervention with an information booklet can help to somewhat gain a

better understanding about anticoagulation therapy for atrial fibrillation.[12]

Barriers Encountered During Counselling:

- Language
- Lack of privacy for counseling
- Elderly patients
- Illiteracy
- Lack of patient interest
- Accessing patients during telephone review.

CONCLUSIONS

The study concluded that pharmacist – provided health education improves the knowledge of patients regarding therapy with Acitrom/ Warf. The ability to recall the provided information is proved to be significantly improving in patients provided with a patient information leaflet. The following conclusions were derived from our study:

- Counselling regarding the acitrom therapy, improved the knowledge of patients by 72%.
- Counselling aid (patient information booklet) along with counselling showed a difference in knowledge between intervention (4%) and control group (12%) during the review.
- Female subjects were observed to retain slightly more information (3%) than males when provided with a booklet.
- The age-wise comparison showed that elderly subjects in intervention (68%) group revealed double retention of knowledge than the control group (32%).
- Comparing the type of information retained by the subjects, it was found that drug information questions were answered(64%) than monitoring information (21%), diet and lifestyle (15%).

Acitrom/Warf Patient Information Leaflet which was prepared as a part of our academic project and has been implemented in Cardiology ward of PSG Hospitals, for inpatients and out patients who are started with or who are already on anticoagulation therapy.

FUTURE STUDIES

- The effect of counselling on medication adherence, which is one of the major issues of OAC therapy, can be studied well by continuing the study for a further duration and carrying out three to four reviews accessing their knowledge retention, adverse events encountered and medication adherence.
- The range of anticoagulant control attained by the provided health education and effect of counselling aid can be studied by INR monitoring and assessing the duration of maintaining a normal range.

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AUTHORS CONTRIBUTION

Conceptualisation of work and its realisation - JSC & LKS
Wrote parts of manuscript, acted as corresponding author-JSC & AK
Data collection- JSC, AK & LKS
Result analysis- JSC & LKS
Critical revision of article- JSC, AK, LKS & PAR

CONFLICTS OF INTEREST

None to disclose.

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