

**CONTINUOUS OUTPATIENT WARFARIN COUNSELING AND ITS EFFECTS ON ADHERENCE**Rana Ibrahim\*<sup>1</sup>, Maha Saber-Ayad <sup>1,2</sup><sup>1</sup> College of Pharmacy, University of Sharjah, <sup>2</sup> College of Medicine, Cairo University, Email : ribrahim@sharjah.ac.ae*Received: 2 January 2013, Revised and Accepted: 6 February 2013***ABSTRACT**

Warfarin is a commonly used anticoagulant, which reduces the occurrence of thromboembolic events. Managing patients on warfarin therapy represents a challenging task for the health team. Many studies showed revealed sub-optimal treatment in a large number of patients that predispose to drug-related problems. Patient awareness and continuous counseling about different aspects of warfarin use should improve the outcome. This is a comparative study evaluating the impact of continuous counseling on the outcome of warfarin therapy and patient satisfaction on 240 patients, recently placed on warfarin therapy. Telephone consultation (once/week) and home visits (2/month) by a nurse or a pharmacist were continued for 3 months in the study group. The control group receives the "usual medical care". Patients in the study group had better control of their International normalized ratio (INR) compared to the control group since 21 patients in the study group had their INR outside the therapeutic range versus 86 patients in the non-counseled group. Number of adverse events was significantly lower in the study group (22 versus 84,  $p=0.015$ ). Patient satisfaction was higher in the study group in form of better understanding and fewer difficulties during the study period. In conclusion, warfarin therapy is a burden on the health system and the patients. Continuous counseling through phone calls and home visits by nurses and pharmacists can improve the outcome in terms of lowering the adverse events and increasing the patient satisfaction.

**Keywords:** International normalized ratio, INR, anticoagulation clinic, warfarin, counseling, adherence, adverse effects**INTRODUCTION**

Clinical trials in the 1990's showed that oral anticoagulation was almost twice as effective as aspirin in preventing strokes in patients with atrial fibrillation (AF) and other cardiac abnormalities <sup>1</sup>. As life expectancy gets longer than ever before, chances are that outpatient oral anticoagulation prescribing will be on the rise.

Many of the anticoagulation patients either visit Anticoagulation clinics (AC) monthly or are followed by the normal standard care with their physician as needed basis. When patients strictly follow their drug-taking instructions, this increases their chance of survival and reduces unnecessary complications. In addition to its established benefit for stroke prevention, effective anticoagulation therapy is associated with decreased stroke severity and better functional outcome and survival in patients with AF presenting with acute brain ischemia <sup>2</sup>.

Improper monitoring or misuse of warfarin can lead to significant problems such as thromboembolic complications, DVT, bleeding complications, or even death. Complicating matters even more, warfarin is involved in many drug-related problems that include dosing, drug interactions, dietary intake, and patient compliance, all of which can dramatically affect its levels <sup>3</sup>.

An important factor to consider with anticoagulation therapy is the level of the patient's knowledge. In a study conducted in London, few patients could correctly identify adverse conditions associated with poor control of anticoagulation and their knowledge of anticoagulation in general was poor <sup>4</sup>. Thrombosis is the "most common single cause of death in the United States" killing more than 2 million patients annually due to arterial/venous thrombosis or their consequence <sup>5</sup>.

Additional studies suggest that the majority of patients being discharged on oral anticoagulation therapy required counseling during a 7-week period <sup>6</sup>. It is obvious that adherence is extremely crucial when it comes to warfarin patients and the cost of healthcare. Combining patient compliance and the adverse drug events with warfarin, managing these patients is not an easy task. Follow-up care at home seems to benefit other patients and the institutions caring for these patients.

The pharmacist can play an important role to improve patient's compliance and minimize drug related problems. Among patients starting warfarin for the first time, daily consultation by a

pharmacist significantly decreased the length of hospital stay and the number of patients who received excessive anticoagulation therapy <sup>7</sup>.

Congestive Heart Failure (CHF) patients that had received follow-up 'care at home' from a cardiac nurse showed a significant reduction of risk of death (33%) and hospital readmission was reduced by 40% when compared with similar patients who got standard care <sup>8</sup>. Furthermore, for CHF patients, an intervention, as simple as phone calls from a nurse can help keep CHF patients out of the hospital and 'lower their medical costs'. The study shows that a low-cost, low-tech method can have positive results. The average number of days spent in the hospital was 46% lower in CHF patients receiving printed educational material, and follow-up phone calls <sup>8</sup>.

An Australian study of a home-based medication review-type intervention by pharmacist showed a 25% reduction in admissions and a reduction in deaths outside hospital <sup>9</sup>. Therefore, taking to consideration the following:

- Many patients that leave the office visit do not understand well, what the doctor said. In most cases, patients do not participate in the decision-making.
- Primary care clinicians have too many issues to deal with in an average of eighteen minutes.
- Adopting health behaviors and achieving good clinical outcomes requires that patients understand their chronic condition and are involved in decision-making.
- When chronic care quality is inadequate, it will cause an increase in hospital visits, injuries or fatalities.
- It is worthwhile to conduct additional consultation (via home visits, phone calls, etc.) for chronic patients receiving oral anticoagulation treatment to reduce hospital re-admissions and improve compliance.

Warfarin patients and their adherence patterns will impact the health system financially by ways of anticoagulation-related Emergency Department (ED) visits and complication management. Although AC's are available in many areas and can help reduce complications and cost, adherence can still be an issue. Shehab et al, 2012 concluded recently that attentiveness and adherence to warfarin treatment and monitoring guidelines are suboptimal among patients and medical staff in the UAE. They suggested that

novel strategies are necessary to alert patients, pharmacists and physicians on the seriousness of warfarin treatment failure<sup>10</sup>.

The current study aims at observing the improvement, if any, of adherence in patients on warfarin who are continuously being counseled either by phone, mail, or periodic home visits by either nurse or pharmacist.

## METHODS

The study compares two groups of 120 patients being discharged for the first time on the oral anticoagulant warfarin (from the DMC medical center). More specifically, the first 240 patients discharged or prescribed for the first time warfarin (regardless of strength, gender, or age) are divided randomly and assigned a certain group. Group A is the "counseled" group, whereas, Group B is the "non-counseled" group. The patients were followed up for 3 months. After initial physician/pharmacist consultation in a standard care setting, one group is thoroughly counseled, defined by the following:

- Once a week telephone consultation reviewing a series of pre-designed set of questions (same questions asked weekly).

- Two home visits per month per patient by either a nurse or a pharmacist (reviewing questions and basic information). Visits are 12-14 days apart, generally.

- Any additional contact as requested by the patient in the intervention group.

The other group received no follow-up consultation other than what was ordered by their own physician in a standard care setting. This group is asked only to visit the anticoagulation clinic twice a month for three months to evaluate INR levels.

A "normal" or "therapeutic" level is between 2-3. Levels above 3.5 (supratherapeutic) or below 2 (subtherapeutic) would be considered outside the desired range and may not be achieved for various reasons including adherence issues. Achieving the planned INR level is the tool to measure therapeutic satisfaction. Adverse effects are noted during the visits and via phone interviews as laid out in the questionnaire.

The questionnaire points out possible reasons for adverse effects (i.e., drug interactions, non-adherence, diet changes, etc.). There is a detailed patient profile recorded that takes into consideration any potential drug interactions that may contribute to "non-therapeutic" INR levels. Also recorded is a patient's dietary intake of any Vitamin K containing products (i.e. green leafy vegetables, etc.) or herbal medications/OTC products. All patients are scheduled for bi-monthly visits to an anticoagulation clinic for INR testing. At the end of the three month study each patient (Group A and B) was given an evaluation form addressing patient satisfaction. This form was filled out by the patient answering questions of their experience including the change in the level of awareness, difficulties with treatment, availability and evaluation of consultation and compliance with life style modifications.

INR levels for all patients in both groups were recorded for comparison and evaluation purposes. The results were examined at the end of the trial period (total of 6 readings/ patient).

The questionnaire was developed in English and validated by 2 physicians, 2 pharmacists and a pilot group of 10 patients. The plan

**Table 2: Comparison of Primary and Secondary Outcomes between the Two Groups.**

Outcomes	Counseled Group A (n = 120)	Non-counseled Group B (n = 120)
Total no. adverse effects*	22	84
No. of pts experiencing adverse effects**	23	75
No. of thromboembolic events	0	41
No. of hemorrhagic events	21	43
No. of hospital days used for warfarin adverse events	5	28
Median length of hospital stay in days*** (mean +/- SD days)	3.2 (2.78±0.85)	3.93 (5.32±3.74)
Admission INR outside therapeutic range	21	86
Subtherapeutic	11	33
Supratherapeutic	10	53

was to have a staff pharmacist conducting the phone interview from his/her regular job where 30 minutes per patient is allocated for the call (prescheduled with the patient). Pharmacist time was incorporated in the normal staff schedule. In addition, the time for the scheduled visits (total 8 visits) by a nurse was also incorporated in the normal schedule allowing 30 minutes per visit. Home visits by the staff nurse were supposed to include reinforcement of information, answering questions, providing further counseling, and verifying treatment (i.e., correct dose, schedule, patient involvement, etc.).

## OUTCOME MEASUREMENTS

The primary outcome data and analysis was the following:

- Percentage of values between 2-3
- Number of adverse effects and events
- Patient satisfaction

## Statistical Analysis

A computer software package (SPSS), version 15, was used in the analysis. For quantitative variables, mean and standard deviation are presented. Frequency and percentage are presented for qualitative variables. Chi square/ Fisher's Exact were used to estimate differences in qualitative variables. An alpha error level of  $p < 0.05$  was considered as statistically significant.

## RESULTS

### Demographics

There was no significant difference between the groups in terms of age, sex, and days in study (Table 1). There was no statistically significant difference found between the groups based on indication for anticoagulation, with atrial fibrillation representing the most common indication. All patients live close to the participating medical center and can access it easily.

**Table 1: Demographics of the study population**

Use of the 240 Patients Evaluated	
<b>A</b>	No (%)
Age (yrs), mean (range)	60.2 (17.84)
Men	140 (58.3)
<b>Primary Indication for Warfarin</b>	
Atrial Fibrillation	82 (34.2)
DVT/PE	65 (27.1)
Valve replacement	37 (15.4)
CHF	32 (13.3)
Peripheral Artery Disease	8 (3.33)
Left Ventricular thrombus	7 (2.91)
Stroke	9 (3.75)

### Anticoagulation Control

As shown in Table (2) analysis of total INR values sub-therapeutic and supra-therapeutic did show statistical difference between the two groups. There were no INR values higher than 6.0 or lower than 1.0. Group B (standard care group) had more values outside (86 patients) the desired range than Group A (21 patients).

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 INR = international normalized ratio
 

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\*p Value=0.0155

\* p Value= 0.0942

\*\*p Value= 0.209

Some patients experienced more than one adverse event

### Adverse Events Related to Bleeding or Thromboembolic Complications

The review of all emergency department visits and inpatient admission data showed 12 inpatient admissions and 11 emergency department visits that were related to complications of oral outpatient anticoagulation therapy in Group A ; compared with 30 inpatient admissions and 33 emergency department visits related to complications of outpatient therapy for Group B (standard care group), table 3.

There is a statistically significant difference between the two groups as regards to the total number of adverse events ( $p=0.015$ ), (some patients experienced more than one adverse event), whereas the numbers of patients experiencing adverse effects did not differ significantly ( $p=0.209$ ), table 4.

**Table 3: Comparison of counseled and non-counseled groups according to the emergency room visits and hospital admissions**

Event	Group A (n=120)	Group B (n=120)
<b>Emergency Room visits</b>		
Warfarin related	11(9.2%)	33(27.5%)
Warfarin non-related	20(16.6%)	24(20%)
Inpatient admissions	12(10%)	30(25%)

**Table 4: Causes of Over and Under-anticoagulation**

Group B (non-counseled) n=120, 84 adverse effects: No (%) of patients

Causes	INR<2	INR>3.5	P-value	95% CI
<b>Dosing issue</b>				
Initiation of therapy	12 (10%)	20 (16.6%)	<0.001	0.06
Warfarin held intentionally			<0.001	0.08
Noncompliance/dosing error	14 (11.6%)	16(13.3%)		0.08
				0.14
<b>Interactions</b>				
Change in prescription drugs		9 (7.5%)	<0.001	0.08
Change in non-prescription drugs	13 (10.8%)			0.02
Change in health status				0.03
Change in dietary vitamin K				0.02
Change in alcohol intake				
Change in activity level				

Note group A: 20 adverse effects due to "health status changes".

**Table 5: Patient Satisfaction Results**

Question#	Group A [No (%)]	Group B [No (%)]
1. "Better understanding"	120(100%)	42(35.0%)
2. "Experienced difficulties"	20 (16.6%)	52(43.3%)
3. "Satisfied with consultation"	110(91.6%)	64(53.3%)
4. "Need extra help"	12 (10.0%)	40(33.3%)
5. "more compliant" with lifestyle modifications	105(87.5%)	41(34.2%)

### Patient satisfaction

As shown in Table (5), there was a significant difference in the feedback results posed as 5 questions to both groups. Group A

patients claimed "better understanding" and experienced "fewer difficulties" with their treatment than the patients in Group B. In addition, they were more "satisfied" and required no further assistance with their treatment. Furthermore, 'Group A' patients claimed more commitment to improve their health (i.e., diet, exercise, less alcohol intake) than patients in Group B.

### Discussion

Oral anticoagulants are among the most notorious drugs as regards to the frequency of adverse events. Proper anticoagulation is crucial to ensure patient safety. Consequences of improper anticoagulation can result in morbidities and mortalities, which are mostly avoidable.

In our study the main indication of anticoagulation was atrial fibrillation (34.2%). Our results are comparable to other studies that showed atrial fibrillation as the main cause of receiving oral anticoagulants<sup>10</sup>. Other studies showed deep venous thrombosis as the main cause of receiving anticoagulants<sup>11,12</sup>.

The data collected in this study suggests that enhanced and specialized care provided by pharmacists/nurses in a home setting and weekly scheduled phone consultations decreased risk of hospitalization for an adverse event associated with anticoagulation. Although the median length of hospital stay did not differ significantly between the two groups, total hospital days (5 vs 28) were higher in Group B (standard care).

Previous studies showed that better anticoagulation control can be obtained in patients visiting AC clinics versus those who receive "usual medical care", but the impact was marginal as indicated by the time taken to achieve the therapeutic range TTR<sup>12</sup>. This was not measured in our current investigation.

A recent cross sectional survey involving 160 patients took place in one of the hospitals in the UAE. The results showed that 80% reported inadequate understanding of the "warfarin booklet" contents, 88% were unaware of warning labels<sup>10</sup>. This shows the need of enhancing patient knowledge about the drug through cooperation of members of medical team including pharmacists and nurses. In our study, results indicated that patients who received intensive counseling showed significantly better understanding compared to the "usual medical care" group. Establishing more AC clinics and training clinical pharmacists in this field seems of utmost importance to improve the current situation.

Our evaluation of this method of bi-monthly pharmacist/nurse home visits plus weekly phone call follow-ups suggest that there is a need for larger scale studies of this kind.

Verret et al, evaluated the impact of a pharmacist-led warfarin patient self-management program on quality of life and anticoagulation control compared to physician-led AC clinics. They concluded that pharmacist-led warfarin patient self-management program resulted in significant improvement in the quality of life, as well as reduction in the time required for anticoagulation monitoring<sup>13</sup>.

An increased number of hospitalizations and increased length of stay ultimately translates into higher overall healthcare costs and a need for enhanced patient care. Coordinated care provided by pharmacists/nurses can have an impact on the financial burden absorbed by both the patient and institutions. In a recent qualitative study, home delivered services and post-discharge management should focus on providing patients with a solid foundation to minimize drug-related problems<sup>14</sup>.

Additional pharmaco-economic analysis and larger scale studies may prove worthwhile as the cost of healthcare continues to rise. The bottom line is that an increase in hospital stay translates into an increase in health care costs. Furthermore, as the general

population continues to age and live longer, more patients will be prescribed oral anticoagulation requiring more consultation.

The implication of such programs in the UAE may achieve the same results if run by highly trained and qualified pharmacists<sup>13</sup>. This can influence the strategic plans of the Ministry of Health and enhance the role and significance of clinical pharmacists.

## CONCLUSION

Pharmacists can play an important role in managing anticoagulation therapy through continuous outpatient counseling. This strategy has a great impact on enhancing appropriate drug use and adherence, minimizing drug-related problems and achieving patient satisfaction.

*The authors declare that there is no conflict of interest.*

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