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Effectiveness of Pharmacy Run Anticoagulation Clinics Compared to Large Clinical Trials of New Oral Anticoagulants

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Abstract

Purpose: The purpose of the study was to assess the quality of anticoagulation with warfarin in patients with non-valvular AF who were managed exclusively in pharmacy run anticoagulation clinics and to evaluate whether these patients would be expected to have the same efficacy and safety profiles as those patients in the RE-LY, ROCKET AF, and ARISTOTLE trials.

Methods: This was a retrospective study of 146 patients in 3 pharmacy run anticoagulation clinics who were initiated on anticoagulation with warfarin therapy to prevent stroke associated with atrial fibrillation. International Normalized Ratio (INR) values were collected over a 1-year period and the quality of management was expressed as time in therapeutic range (TTR) calculated by Rosendaal's linear interpolation method.

Results: Forty-six patients from university internal medicine (UIM) clinic, 9 patients from family medicine (FM) clinic, and 91 patients from pharmacotherapy (PCT) clinic were studied. During the 1-year period, the overall mean TTR was 61.1%. The mean TTR in the UIM clinic, the FM clinic, and the PCT clinic was 60.1%, 62.5%, and 61.5%, respectively.

Conclusion: The quality of anticoagulation with warfarin, as assessed by TTR, in the 3 pharmacy run anticoagulation clinics was similar to the mean TTR values reported for the warfarin-treated patients in the RE-LY, ROCKET-AF, and ARISTOTLE trials. The results of these studies are applicable to our patient population.

Keywords: Anticoagulation; Pharmacotherapy; Atrial fibrillation

Background

One of the major complications associated with atrial fibrillation (AF) is stroke, accounting for approximately 10-15% of all ischemic strokes in patients greater than 65 years of age and approximately 25% of all ischemic strokes in patients greater than 80 years of age [1]. It can be prevented by lifelong use of oral anticoagulation therapy. Until recently, warfarin, a vitamin K antagonist, was the mainstay therapy for prevention of stroke in these patients. Warfarin's effectiveness has been demonstrated in several randomized clinical trials for primary prevention of stroke with a mean 66% reduction in the risk of stroke [2-7]. However, its limitations, including the side effect profile, narrow therapeutic index, numerous drug/food interactions and need for frequent monitoring, have led to the development of new oral anticoagulation therapies that would be safe and effective alternatives to warfarin [8-10].

So far, three new oral anticoagulation therapies have been compared to warfarin in large phase III clinical trials. These include the oral direct thrombin inhibitor, dabigatran etexilate and the two oral Factor Xa inhibitors, rivaroxaban and apixaban. Of these, dabigatran, rivaroxaban, and apixaban have been FDA approved for stroke prophylaxis in patients with atrial fibrillation.

In RE-LY trial, dabigatran 150 mg BID was superior to warfarin for the primary endpoint of stroke and systemic embolism with similar rates of major bleeding events [11]. In ROCKET-AF trial, rivaroxaban 20 mg once daily was non-inferior to warfarin for stroke and systemic embolism with similar rates of major bleeding events [12]. In ARISTOTLE trial, apixaban 5 mg BID was superior to warfarin for reducing stroke and systemic embolism with 31% fewer major bleeding events [13].

The average TTR values in the warfarin-treated patients for RE-LY, ROCKET-AF, and ARISTOTLE were 64%, 55%, and 62% respectively [11-13]. In these 3 trials, TTR for warfarin have varied. In assessing the safety and efficacy of new oral anticoagulants compared to warfarin at the Medical University of South Carolina (MUSC), time in therapeutic range (TTR) of patients managed by pharmacists in pharmacy run clinics needed to be measured in order to apply these trial results to MUSC's patient population.

Methods

This was a single-center retrospective cohort analysis assessing TTR of non-valvular AF patients receiving warfarin in the pharmacy run anticoagulation clinics at MUSC and evaluating whether these patients would be expected to have the same efficacy and safety profiles as those patients in the Re-LY, ROCKET-AF, and ARISTOTLE trials. The study was initiated after approval from MUSC's institutional review board. A list of warfarin orders for atrial fibrillation was generated through reports from EPIC, MUSC's outpatient electronic medical record system, and reviewed for inclusions and exclusion criteria. All patients 18 years of age or older who received warfarin for stroke prevention for non-valvular AF from an MUSC pharmacy run anticoagulation clinic for more than 2 months on June 1, 2012 were considered eligibile for inclusion in the study.

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This study did not affect any patient's present or future course of therapy, therapy regimens, or outcomes. Data was collected on a standardized data collection form. Any ages reported as results were reported as age ranges, as specified on the data collection form submitted for IRB approval. All data were de-identified prior to analyzing the data and reporting any results. Data analysis was performed using descriptive statistics and TTR was calculated based on Rosendaal's linear interpolation method [14].

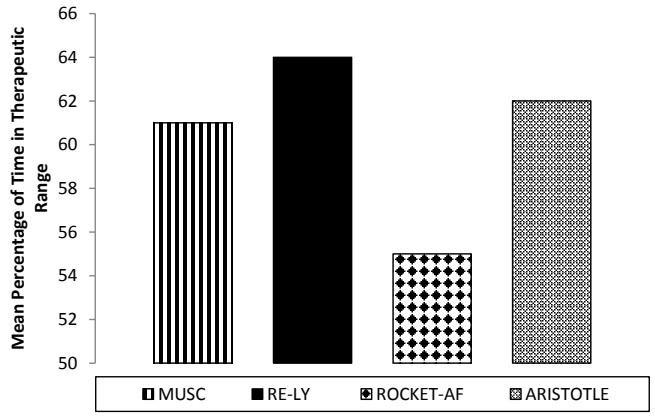
Results

A total of 146 patients were identified for inclusion, of which 46 patients were from the university internal medicine (UIM) clinic, 9 patients were from the family medicine (FM) clinic, and 91 patients were from the pharmacotherapy (PCT) clinic. Patients were mostly elderly, male, and white, although the racial diversity differed by site (Table 1). The mean duration of follow-up was 10.8 months.

Patients averaged 10.3 INR tests during follow-up, and approximately one-third of the test results prompted dose adjustments. The mean percentage of time patients spent within the target INR range of 2 to 3 was 61.1%, with little variation by clinics (60.1% for the UIM clinic, 62.5% for the FM clinic, and 61.5% for the PCT clinic) (Figure 1). More time was spent below the mean target range (21%) than above it (17%) (Figure 2).

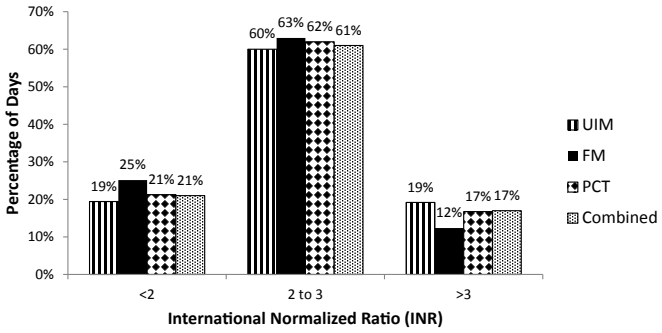
Characteristic	UIM Clinic (n = 46)	FM Clinic (n = 9)	PCT Clinic (n = 91)
Age (yrs), %			
18-30	0	0	0
31-50	0	0	4
51-75	61	100	48
>75	39	0	48
Male, %	46	78	60
Race, %			
African American	50	89	31
White	48	11	64
Other	2	0	5
Months of follow-up, mean	11.4	10.5	10.4

Table 1: Characteristics of Study Patients.



The mean percentage of time spent within the target INR range of 2 to 3 for the patients receiving warfarin therapy at the Medical University of South Carolina (MUSC) outpatient clinics, and for the patients receiving warfarin therapy in RE-LY, ROCKET-AF, and ARISTOTLE clinical trials.

Figure 1: Mean time in therapeutic range (TTR) values for the Medical University of South Carolina (MUSC) outpatient clinics vs. 3 Phase III clinical trials.



The mean percentage of time in days spent within the target INR range of 2 to 3, below the target of 2, and above the target of 3 for patients receiving warfarin therapy in the 3 different outpatient clinics of the Medical University of South Carolina (MUSC). UIM = university internal medicine clinic, FM = family medicine clinic, and PCT = pharmacotherapy clinic.

Figure 2: Distribution of percentage of days patients spent within specified INR intervals.

Discussion

In this study, we found that the level of anticoagulation control (percentage of days within INR therapeutic range) averaged 61%. The levels of anticoagulation control were quite similar across the sites.

The quality of anticoagulation control that was observed in this study is somewhat higher than that reported in several other observational studies conducted in anticoagulation clinic settings, where TTR varied from 40% to 60% [15-17]. The largest of these studies used data from 144 patients enrolled across 5 managed care organizations to estimate that INRs in patients with non-valvular atrial fibrillation were within the target range approximately 56% of the time after the patients participated in an anticoagulation service intervention program [17].

The TTR in the pharmacy run clinics (61%) was similar to the mean TTR values reported for the warfarin-treated patients in the RE-LY, ROCKET-AF, and ARISTOTLE trials, with the average TTR values being 64%, 55%, and 62% respectively [11-13].

There were several limitations to this study. First, the data were collected retrospectively and were dependent on appropriate documentation and consistent data collection amongst all the investigators. Additionally, the data for this study were collected at a single study site with a limited population. Finally, this study was not designed to assess the safety of warfarin therapy and therefore, the number of bleeding and thrombolic events were not collected.

Conclusion

Based on the data from the 3 pharmacy run anticoagulation clinics at MUSC, this study found that the quality of anticoagulation remains suboptimal. However, it is similar to the TTR values reported for the warfarin-treated patients in RE-LY, ROCKET-AF, and ARISTOTLE trials. Additionally, the results from this landmark, phase III clinical trials should be applicable to the MUSC patient population.

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