J Thromb Thrombolysis (2012) 33:173–177
DOI 10.1007/s11239-011-0642-1

Potential benefits of warfarin monitoring by a clinical pharmacist in a long term care facility

Carol Motycka · Carl Kesgen · Steven M. Smith · Edgar Alvarez · Kelly Jones

Published online: 2 October 2011

Abstract The primary objective of this study was to determine whether warfarin therapy monitoring by a pharmacist would benefit a long-term care facility, by maintaining patients within therapeutic INR range more consistently than the current practice of physician monitoring.Secondary objectives included whether adverse events resulting from non-therapeutic INR levels differed significantly between groups and whether pharmacist interventions resulted in decreased overall costs to the facility. A retrospective chart review was conducted on all patients treated with warfarin for a minimum of 14 days within a Long-Term Care (LTC) facility to compare Time within Therapeutic Range (TTR) between staff treated patients versus pharmacist treated patients. A total of 552 INRs were obtained for all patients during the study period: 499 (90.4%) under staff supervision and 53 (9.6%) under clinical pharmacist supervision. Of the 499 tests performed by the River Garden staff, 203 were within the desired range, compared with 29 of the 53 tests performed by the clinical pharmacist being in range. For the primary endpoint, a total of 1483 INRs were imputed, corresponding to the number of days between true INR measurements. INRs attributable to clinic staff management were within the therapeutic range 47.1% of the time, whereas INRs attributable to clinical pharmacist management were within the therapeutic range 58.7% of the time ($P < 0.0001$ for the comparison). Warfarin can be effectively monitored by a clinical pharmacist and routinely lead to appropriate INR levels in the nursing home setting, while potentially saving the facility healthcare dollars.

Keywords Anticoagulation services · Pharmacist monitored · Long-term care · Cost savings

Abbreviations

ACCP	American College of Chest Physicians
INR	International Normalized Ration
LTC	Long Term Care
TTR	Time within Therapeutic Range

Objective

Guidelines published by the American College of Chest Physicians (ACCP) and adapted by the American Geriatrics Society recommends warfarin use in elderly patients with chronic atrial fibrillation, prosthetic heart valve replacement, and recent thromboembolic events [1, 2]. More than 1.6 million Americans currently reside in nursing homes and it is estimated that nearly 200,000 of these residents receive warfarin therapy [3]. Given these figures, the increasing number of elderly citizens in the population, and the age-related increase in the prevalence of disease states requiring chronic anticoagulation, we can expect prescribing trends will reflect the rising need for warfarin therapy.

C. Motycka (✉) · K. Jones
University of Florida, 580 W. 8th Street, Jacksonville, FL 32209, USA
e-mail: Motycka@cop.ufl.edu

C. Kesgen · E. Alvarez
River Garden Hebrew Home, Jacksonville, FL, USA

S. M. Smith
Department of Clinical Pharmacy, School of Pharmacy, University of Colorado Denver, Denver, CO, USA

Warfarin therapy is associated with a narrow therapeutic index and high inter-individual variability in dose response, which have made its use in the elderly challenging [4]. Changes that occur in the normal aging process exacerbate these issues and can lead to an increased sensitivity to the anticoagulation effects of the drug [4]. Specific pharmacodynamic concerns in the elderly include greater inhibition of the synthesis of vitamin K-dependent clotting factors, while pharmacokinetic concerns involve a decrease in plasma protein binding by 15% to 25%, leading to increased free plasma levels of highly protein bound drugs such as warfarin [4].

Numerous studies have illustrated challenges associated with warfarin therapy. Many of these have shown that pharmacist interventions are successful in improving anticoagulation outcomes and decreasing costs. Witt et al., studied the subsequent results following the implementation of a clinical pharmacy anticoagulation service [5]. This 6 month study demonstrated that the pharmacy service reduced anticoagulation therapy complications, with the greatest reductions seen in thromboembolic complications compared to the group monitored by physicians' alone [5]. Poon et al. [2] examined the effects of pharmacist-monitored anticoagulation therapy in patients over the age of 75. The results once more showed significantly reduced thromboembolic events compared with the physician monitored group [2]. Another study by Burns also focused on warfarin dosing initiated by pharmacists in elderly patients [6] Patients enrolled in this study were an average of 81 years of age, and pharmacists managing their therapy more often gave appropriate loading and maintenance doses compared to physicians [6]. Additionally, pharmacists were found to be more thorough in documenting pertinent patients' monitoring information, which may have contributed to more expeditious attainment of International Normalized Ratio (INR) goals and fewer INR assessment tests [6].

Costs associated with outpatient pharmacy anticoagulation services have also been investigated. A study by Anderson found that quality warfarin control was obtained at a cost of $62.30 total per-patient-per-month which included the pertinent medications, INR tests, and clinical pharmacy specialist fees [7]. Warfarin control was measured by time spent in the target INR range, which is associated with a decreased risk of stroke, bleeding and death [7]. Patients having lower incidences of major complications led to overall lower healthcare costs, which in turn offset the cost of monitoring services pharmacists could provide [7]. Chiquette et al. [8] examined a clinical pharmacist supervised anticoagulation clinic and found an annual savings of $132,086 per 100 patients treated, owing specifically to decreased warfarin-related hospitalizations and emergency department visits

Newer oral anticoagulants, including the oral direct thrombin inhibitor dabigatran, may jeopardize the future use of warfarin [9]. However, there is a tremendous difference between monthly medication costs of these two drugs. A 1 month wholesale acquisition cost of warfarin 5 mg tablets costs approximately $13.99, while a one-month supply of dabigatran 75 mg or 150 mg capsules is estimated at $202.50 [10, 11]. Despite the sizeable differences in price, the notion that warfarin therapy and its monitoring is too dangerous, tedious, or costly has led many clinicians to believe this effective drug option should be abandoned. However, when used in a controlled and responsible manner, warfarin therapy continues to be highly efficacious and inexpensive.

The primary objective of this study was to determine whether warfarin therapy monitoring by a clinical pharmacist would benefit a long-term care facility, by maintaining patients within therapeutic INR range more consistently than the current practice ofstaff monitoring, which included physicians and nurse practitioners.

Secondary objectives included whether adverse events resulting from non-therapeutic INR levels differed significantly between groups and whether clinical pharmacist interventions resulted in decreased overall costs to the facility.

Design/setting/particpants

A retrospective chart review was conducted on all patients treated with warfarin within a long-term care (LTC) facility between the dates March 1, 2008 and February 29, 2009. Eligible patients received a warfarin regimen for a minimum of 14 days and had at least one INR measurement during their treatment. Patients who had not received warfarin for at least 14 consecutive days, those who had been admitted to a hospital during the study period, and those who required permanent discontinuation of warfarin therapy for any reason were excluded. Pertinent data was collected from eligible patients for the 6 months prior to and 6 months after implementation of warfarin monitoring by a clinical pharmacist. In addition to recording INR values, each chart was thoroughly examined in order to discover any pertinent information regarding warfarin therapy that may have been written by the clinician at the time monitoring was performed. This information was found in four possible sections within the medical chart: 'New Order, Significant Finding/AE (adverse event), Physician's Progress Notes, and Physician's Orders'. This information supplied the nursing staff with instructions about the administration of warfarin. It also provided reasoning for dosage adjustments made by the clinicians in response to subtherapeutic and supratherapeutic INR values. Any suspected causes the clinician attributed these deviations to,

such as food-drug interactions or drug–drug interactions, were also recorded. The INR values and the supplementary data from each chart were used to determine study outcomes, including how often INR values were within range (the range was 2–3 for all patients studied and baseline INRs were not included), how frequently clinicians choose to obtain this value, and any adverse events which would indicate supratherapeutic or subtherapeutic INR values such as vitamin K administration, blood transfusions, held doses, bleeding events, pulmonary emboli, deep vein thrombosis or thromboembolic events. The number of blood samples drawn to maintain the INR within goal range and any adverse events, was used to determine what cost savings clinical pharmacist monitoring might provide a long term care facility. All data obtained during the study was recorded using a Microsoft Excel spreadsheet. IRB approval from the LTC facility was given on September 1, 2009.

Statistical analysis

The primary endpoint in this study was time within the therapeutic range (TTR). The Rosendaal linear interpolation method was used to estimate INR control between clinic visits during continuous warfarin monitoring. Continuous warfarin monitoring was defined as periods of monitoring in which real INR values were determined no more than 30 days apart. Thus, INR imputation was not performed during any period in which a patient had two consecutive INR measurements > 30 days apart. To compare TTR for anticoagulation management performed by clinic staff versus a clinical pharmacist, individual patient INRs were attributed to clinic staff management or clinical pharmacist management according to who had managed the anticoagulation therapy at the most recent previous visit. For example, an individual INR level (and any imputed INRs) was attributed to clinic staff management only when clinic staff had managed anticoagulation at the patient's previous visit, regardless of who managed it at the present visit.

Descriptive statistics were used to identify baseline characteristics of enrolled patients. We tested for differences between pharmacist and staff management using the Chi-squared test or Fischer's exact test for categorical data.

We defined statistical significance a priori as a P-value < 0.05. All statistical analyses were performed with SAS 9.2 (SAS Institute, Cary, NC) or R 2.12.0 (R Development Core Team, http://www.r-project.org) statistical software.

Results

Seventeen patients were identified as potential study participants. Of those identified, ten patients were excluded from the study due to insufficient data in the medical chart according to the study protocol. Thus, seven patients fully met the inclusion criteria and were enrolled in the study.

INRs were obtained, on average, once every 3.5 days when patients were managed by clinic staff, compared with approximately once every 7 days under pharmacist management.The clinical pharmacist monitored the same patients, however, tests were given approximately once weekly. A total of 552 INRs were obtained for all patients during the study period: 499 (90.4%) under staff supervision and 53 (9.6%) under clinical pharmacist supervision. Of the 499 tests performed by the River Garden staff, 203 were within the desired range, compared with 29 of the 53 tests performed by the clinical pharmacist being in range. For the primary endpoint, a total of 1483 INRs were imputed, corresponding to the number of days between true INR measurements. INRs attributable to clinic staff management were within the therapeutic range 47.1% of the time, whereas INRs attributable to clinical pharmacist management were within the therapeutic range 58.7% of the time ($P < 0.0001$ for the comparison; Fig. 1).

Of the 499 tests requested by the staff, 59 (11.8%) of the values were supratherapeutic (see Table 1). In 33 (55.9%) of these instances, at least one dose was held. Of the 53 tests conducted while the clinical pharmacist was monitoring therapy, 9 (16.9%) were elevated, with 3 of the doses subsequently being held. Using the imputed daily INRs, patients spent significantly less time subtherapeutic when managed by the pharmacist (29.07% of days spent

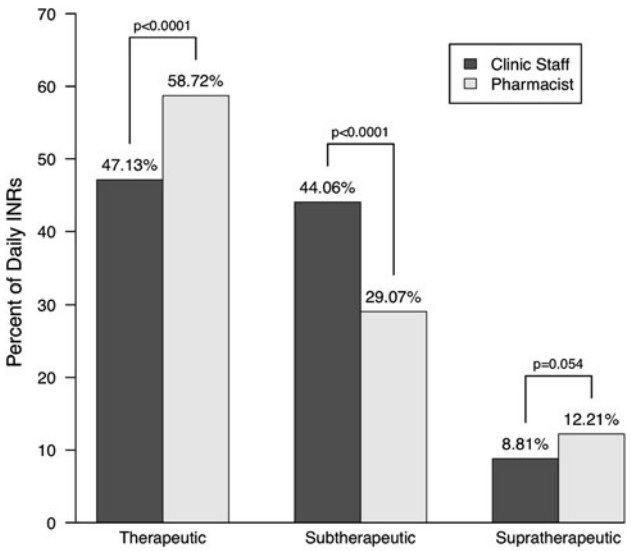

Fig. 1 Percent of daily INRs spent therapeutic, subtherapeutic, or supratherapeutic according to healthcare provider

Table 1

Results	Physician/ staff	Clinical pharmacist
Total number of INRs tested	499	53
Number of INRs within range	203	29
Percentage of true INRs within range	45.50%	54.70%
Number of supratherapeutic INRs	59	9
Number of held doses secondary to elevated INR	33	3
Number of additional INRs ordered	86	2

subtherapeutic) compared with staff management (44.06% of days spent subtherapeutic; $P < 0.0001$ for the comparison), as shown in Fig. 1. No significant difference was observed in the proportion of time spent supratherapeutic (8.81% vs. 12.21%, respectively; $P = 0.0539$ for the comparison between groups)

Discussion

The cost savings of reduced INR testing frequency in elderly patients has been studied and confirmed [7]. It has also been found that improved warfarin control could potentially lessen the incidence of adverse events and complications, such as stroke and emergency department visits, that arise when therapy is not optimal [6]. Other authors studying warfarin therapy in the elderly have found a decreased incidence of thromboembolic events with the implementation of pharmacist monitoring [2, 5]. Although our study did not address major clinical outcomes of anticoagulation therapy, our findings of improved TTR in pharmacist-managed patients suggest that similar benefits might be achievable in LTC patients requiring chronic anticoagulation.

The agreement to bring in a clinical pharmacist by the facility staff to assist with warfarin monitoring was based on the potential for improving quality of care. This was demonstrated by evaluating the percentage of INRs within therapeutic range and subsequent held doses when patients were cared for by the clinical pharmacist compared to the staff. We found that anticoagulation management in a LTC facility by a clinical pharmacist resulted in a higher TTR (58.7%) compared with management by clinic physicians and other staff (47.1%)." Additionally, in response to supratherapeutic INR values approximately 56% of scheduled doses were subsequently held by the staff versus the clinical pharmacist who only held roughly 33% of scheduled doses. It is of importance to note although the pharmacist kept the INRs within range for a greater percentage of tests which would ultimately lead to a decreased need for held dosages, the staff at the facility also tended to hold doses at much lower INRs than the clinical pharmacist leading to greater numbers of daily INR checks occurring subsequently. For example, warfarin was at times held for patients with INRs less than 3.3 with no apparent bleeding when reviewed by the staff followed by daily INR tests. Aside from supratherapeutic INRs, no other adverse events were documented within the patient charts during the study period. However, given the fact that adverse events and complications of the disease increase when the INR is out of therapeutic range, the potential for an adverse event was likely increased when monitoring was performed by the staff versus the clinical pharmacist. This is an area in which additional research could be completed in order to show clear evidence of preventing potential adverse events.

The secondary objective was to study cost savings, secondary to the clinical pharmacist warfarin monitoring. The pharmacist was able to maintain a higher percentage of patients at therapeutic levels while requesting the INR be tested weekly versus the staff at the long term care facility who regularly tested two times each week. This could partly be due to the issue clinicians may face when testing too often. Since changes in warfarin doses take anywhere from 5–10 days to produce the ultimate INR reading, testing every 3–4 days can lead to a "chasing the tail" effect in which doses are continuously being changed before full effect has been demonstrated by the drug. Furthermore, since the facility implemented daily testing of supratherapeutic INRs, this caused additional testing to be completed for patients with INRs outside the therapeutic window producing additional costs. While data regarding this aspect of cost savings was not analyzed, clearly maintaining patients within the therapeutic range more consistently results in fewer tests being requested and performed. While each test was obtained by the long term care facility at a cost of roughly ten dollars, the cost for nursing staff time to provide testing should also be considered in larger picture of potential cost savings by the clinical pharmacist.

There were certainly limitations to the study. The sample size was small. This is in part due to the fact that the facility is not very large (total of 180-beds)and many patients tend to be transient (approximately 50-beds for short-term rehabilitative patients)Therefore, relatively few patients met all of the inclusion/exclusion criteria. However, by studying percentages of INR tests, a reasonable conclusion may be applied to the clinic as a whole. Also, this was a retrospective study, therefore, not all of the adverse events may have been documented in the chart. This is not of great concern since adverse events for both the pharmacist and staff monitored patients were both equally likely to have had these possible omissions.

Conclusion

Our study found that warfarin monitoring conducted by a clinical pharmacist at a nursing home facility more consistently maintained INR levels within therapeutic range when compared to monitoring performed by other healthcare providers, while decreasing the costs associated with testing. Through decreased testing frequency, the pharmacist likely decreased the overall cost of managing patients receiving warfarin therapy. These findings support and contribute to evidence from studies conducted previously, examining similar questions. The one unique aspect of our study was our patient population who were residing in a nursing home setting. As the population continues to age and the swell of baby boomers continues entering nursing homes, these results are extremely important and timely.

Warfarin has a narrow therapeutic index and is subject to many drug–drug and drug-food interactions [4]. This coupled with pharmacodynamic changes that occur in the elderly often lead to increased sensitivity to the effects of the drug, including increased bleeding risk [4]. However, this study has helped to demonstrate that warfarin can be effectively monitored by a clinical pharmacist and routinely lead to appropriate INR levels in the nursing home setting. As the population ages, the prevalence of disease states requiring anticoagulation will increase, and a clinical pharmacist is uniquely positioned to provide patients and healthcare facilities with efficient and appropriate medical management of these disorders.

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