Evaluation of a Pharmacist-Managed Anticoagulation Clinic – Improving Access and Patient Care

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Word Count (body): 2043
Word Count (abstract): 300
Funding for the AMS Program was provided by the
Health Innovation Fund, Alberta Health & Wellness.

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Conflict of Interest Notification Page

The authors have no conflicts of interest to declare.

ABSTRACT

Background: Our Anticoagulation Management Service (AMS) is a pharmacist-run ambulatory clinic with a physician advisory committee, serving a quaternary care referral service often referred patients with complicated anticoagulation histories. The purpose of this paper was to assess the hypothesis that our AMS would provide quality anticoagulant control, and prevent thromboembolic and hemorrhagic events, superior to that achieved during a lead in control period of standard care. The use of healthcare system resources was also compared prior to and during AMS care.

Methods: Consecutive patients managed at least four months prior to and following referral to the AMS were included. The primary endpoint was adequacy of anticoagulation (target INR $\pm$ 0.5). Adverse events requiring an emergency department (ED) visit or hospitalization, were classified by ICD codes as thromboembolic, hemorrhagic, or non-anticoagulant related. Healthcare system resource consumption in terms of number of hours spent in the ED and hospitalization costs were compared prior to versus during AMS care.

Results: A total of 125 patients were included, 58% were male with a mean age of 63 $\pm$ 15 (SD) years. Indications for warfarin were atrial fibrillation (40%), mechanical valve replacements (24%), and venous thromboembolism (19%). Adequacy of anticoagulant control was significantly greater in AMS care relative to prior to referral, with patients being in range 69% versus 49% of the time, respectively ($P<0.0001$). Significantly fewer thromboembolic events occurred during AMS care compared with before (4 and 55, respectively; $P<0.0001$) and there was a trend towards fewer hemorrhagic events (17 and 28; $P=0.25$). During AMS care savings included 572 hours in the ED and $122,145 in hospitalization costs.

Conclusions: A pharmacist-directed, physician supported AMS program achieved better INR control and patients experienced fewer hemorrhagic events with significantly reduced rates of clotting complications compared with standard care. Resource utilization was substantially reduced during AMS care.

INTRODUCTION

Warfarin is used for the prevention and treatment of thromboembolic diseases.[1] Therapy is only safe and efficacious when maintained within a narrow therapeutic window, as measured by the International Normalized Ratio (INR). Failure to adequately anticoagulate patients consistently predicts thromboembolic events (e.g., stroke or pulmonary embolism), while patients anticoagulated excessively are at risk of bleeding.[2,3] Managing therapy within this narrow window is complicated by numerous factors including drug interactions, acute and chronic diseases, diet, and inter-individual variability in responding to warfarin.

Given the complexities of effectively delivering warfarin therapy, it is not surprising that literature consistently reveals it is underused amongst patients who could benefit from it,[4,5] and it is often sub-optimally managed when it is prescribed.[6] Accessible, coordinated, and systematic approaches to delivering this therapy, as offered by an Anticoagulation Management Service (AMS), have improved both the use[7] and control of warfarin therapy.[8-12]

While AMSs are common in the United States, they are only just beginning to gain acceptance in Canada. Our AMS was initiated in 2001 as a pilot project with seed funding provided by Alberta Health and Wellness. This AMS is somewhat unique in the Canadian setting because all of the direct patient care is provided by pharmacists that have an extended scope of practice and work in consultation with specialist physicians.[13] We feel this extended scope of practice is the kind of innovation necessary to optimize care delivery in an over-burdened healthcare system. In fostering an interdisciplinary care model, it was extremely important to conduct a thorough evaluation of the impact of the AMS on anticoagulant control, clinical events, and resource utilization. The purpose of this paper is to assess the adequacy of

anticoagulation, rates of anticoagulant-related events and associated healthcare resource utilization for patients prior to and following referral to our AMS.

METHODS

All patients managed by the University of Alberta Hospital AMS between April 2001 and December 2003 that were prescribed warfarin prior to being referred were considered for study. To be eligible, patients had to be prescribed warfarin for at least 120 days prior to and following referral to the AMS. As a new clinical service, it was not felt that randomization of patients was possible. As such, we used a before-after design for evaluation.

The detailed design of the AMS program has been published previously.[13] This innovative program was funded by Alberta Health and Wellness through the Health Innovation Fund. Patients were accepted to the AMS provided they had a legitimate indication for warfarin therapy in accordance with the American College of Chest Physician guidelines,[1] could attend at least one clinic appointment, were accessible for follow-up, and either the patient or the caregiver had the capacity to understand the condition and implications of anticoagulant therapy. The research protocol was approved by the Human Research Ethics Board at the University of Alberta Hospital.

Once referred to the AMS, patients received a standardized educational session and information package. This session informed the patient of the role of the AMS in their care, the need for compliance with therapy and blood tests, and importance of contacting the AMS with any changes that may impact their therapy. Further, the risks and benefits of warfarin therapy as well as factors that may impact warfarin therapy (drugs, diet, alcohol) were explained. An awareness of signs and symptoms indicative of hemorrhagic and thromboembolic complications

were also addressed. Following this initial visit, the anticoagulation management for the patient is assumed by the AMS. With each INR drawn, patients are contacted by phone by a pharmacist, an assessment is performed, warfarin dosing instructions are given, and patients are scheduled for the next INR test date.

The adequacy of anticoagulation was assessed by measuring the proportion of time that patients spent within their desired INR range (target INR $\pm$ 0.5 units) and expanded INR range (target INR $\pm$ 0.7), using the method developed by Rosendaal and colleagues.[14] The first 30 days of management prior to and following referral to the AMS were omitted to allow for initial stabilization. INR results for patients prior to referral were derived from the Regional Laboratory Services database using Personal Health Numbers, with data being retrieved from November 2000 (six months prior to the AMS accepting the first patient for management) to December 2003. Only patients having INRs done within the Capital Health Region were captured for this analysis.

For the event analysis, the entire duration of follow-up prior to and during AMS care was used to capture events. International Classification of Diseases (ICD-9 and later, 10) coding for all instances of emergency department (ED) presentations and hospital admissions on all patients referred to the AMS between April 2001 and December 2003 for the period from November 2000 (i.e., 6 months prior to the first referral in April of 2001) to the end of December 2003 were retrieved. Personal Health Numbers were used to track health system utilization recorded in the Capital Health Region database. Data collected included the date of admission/discharge, diagnoses, length of stay in hours for ED and inpatient days for hospitalization, and an indicator of the cost of the inpatient event called the "Resource Intensity Weight" (RIW). All ED visits and hospitalizations were reviewed by a single investigator and a health records analyst to

classify each presentation as hemorrhagic, thromboembolic, or non-anticoagulant related in accordance with the ICD coding. For ED visits the primary diagnosis was used, whereas for hospitalizations the most responsible diagnosis was used. At the time of event classification, the management strategy (before or during AMS care) was not known.

To assess healthcare resource consumption, the number of hours spent in the ED was captured. For all hospitalizations, the RIW, which measured the resources required for each hospitalization was used. The Capital Health Region has allocated a cost of $3500 for one RIW. Using this, the costs of hospitalizations prior to and during AMS care were computed.

A paired t-test was used to compare the adequacy of anticoagulation prior to and during AMS care. Event comparisons prior to and during AMS care were done using log-linear regression models of correlated data.

RESULTS

A total of 125 patients met the inclusion criteria for this analysis. The mean patient age was 62.9 $\pm$ 15.0 years ($\pm$SD), and 57.6% were male (Table 1). The majority of patients had atrial fibrillation (40.0%), mechanical valve replacements (24.0%) and venous thromboembolism (19.2%) as the primary indication for warfarin.

The mean proportion of time patients were in their actual INR range prior to referral was 48.8 $\pm$ 23.6% whereas during AMS care, time in INR range was 66.5 $\pm$ 16.3% ($P<0.0001$) (Table 2). Using the expanded range, adequacy of anticoagulation increases to 65.3 $\pm$ 22.3% prior to referral and 81.7 $\pm$ 12.5% during AMS care ($P<0.0001$). To address whether the study group of 125 patients were representative of the larger population of patients requiring anticoagulant therapy, we compared this cohort of patients with those ineligible for this analysis. Relative to

these 502 patients, similar demographics (Table 1) and time in therapeutic range (Table 3) were identified.

Over a mean follow-up period of 10.7 months prior to and during AMS care, significantly more ED presentations and hospitalizations for thromboembolic events occurred prior to referral (35.8 and 13.4%/patient year) compared with during AMS care (2.7 and 0.9%/patient year; $P<0.0001$ and $P=0.0080$, respectively) (Table 4). While fewer hemorrhagic ED presentations and hospitalizations occurred during AMS care (10.8 and 4.2%/patient year) compared with prior (18.8 and 6.3%/patient year, respectively), this was not statistically significant. During AMS care, for both thromboembolic and bleeding complications, patients had fewer presentations and spent fewer hours in the ED (61 and 512 hours less, respectively) (Table 5). Similarly, the number and cost of hospitalizations for both thromboembolic and bleeding complications during AMS care was substantially lower ($12,762) compared with that prior to referral ($134,910). Further, patients had substantially more non-anticoagulant related presentations to the ED and hospitalizations prior to referral (323 and 115) compared with during AMS care (137 and 48, respectively).

DISCUSSION

Management of patients under AMS care compared with that prior to referral revealed substantive improvements in patient care. Patients were within their desired INR range significantly more during AMS care, compared with prior to referral. Significantly fewer thromboembolic events occurred during AMS care compared with prior, with a trend towards reduced hemorrhagic events.

Overall, AMS care substantially reduced the use of healthcare system resources. For the 125 patients, prior to referral to the AMS, an additional 572 ED hours and $122,144.95 for hospitalizations was consumed for anticoagulation-related events. Given the average follow-up of 10.7 month prior to and during AMS care, the monthly savings conferred by AMS care for these anticoagulant-related events were 53 ED hours and $11,415 in hospitalization costs. Interestingly, there were also striking reductions non-anticoagulant related events occurred in that during AMS care, with 1225 fewer ED hours and $526,005.20 less in hospitalization costs. While the AMS cannot claim causal inference for the non-anticoagulant related events, it must be recognized that the clinic is in constant contact with these patients, and is likely to be the first to identify changes in general health, and suggest measures to mitigate progression.

Comparing our data to the literature, the adequacy of anticoagulant control within our AMS population is comparable.[8-12] Time in therapeutic range for other AMSs varies from 59% to 89% of the time, depending upon the population evaluated. Our rates may be on the lower end of this range because our AMS is situated within a quaternary referral centre, and largely receives referrals from subspecialists for patients that have had poor anticoagulant-related outcomes or have been poorly anticoagulated in the past. This is verified by the higher rate of events observed in our population. Combining anticoagulation and non-anticoagulation-related events, prior to referral there were 4.7 events per patient year whereas during AMS care only 1.9 events per patient year followed. Despite the impressive reduction observed under AMS care, these data highlight that each patient under AMS care still used our acute healthcare system twice per year.

The rates of thromboembolic events, compared with prior studies of AMSs (4.8% per patient year managed) and routine anticoagulation management (8.1% per patient year

managed), were lower during AMS care and substantially higher prior to referral to our program.[15] This is, in part, likely due to the types of patients referred to our AMS – a referral bias for patients with poor outcomes with anticoagulant therapy or complicated comorbidities that are sent to our program. Although the rate of major bleeding was not significantly different prior to and during AMS care, it was higher than that reported in the literature for AMSs (4.6% per patient year managed). The rate of major bleeding for AMS care fell within that reported for routine anticoagulation management (7.4-18% per patient year managed), although the rates prior to referral were higher than that reported in the literature. Little difference in rates of bleeding over the two time intervals was anticipated as data during AMS care shows patients are more likely to be supra-therapeutic (or therapeutic) relative to prior to being referred. The relatively high bleeding rates in our population is likely a reflection of patient selection in utilizing a specialty service.

There are a few limitations to this study. Firstly, a before-after design was necessary to evaluate this pilot program. Randomization was not feasible because the majority of patients had problematic management or outcomes prior to being referred to our specialty service. Secondly, our data is limited in that it has a relatively small sample size. We applied strict inclusion criteria to comprehensively evaluate INR control and associated outcomes – this resulted in only 125 patients being eligible, but, demographics and INR control are similar to the whole population. Therefore, it seems reasonable to assume these data are reflective of our entire clinic population.

The findings of this study demonstrate that a pharmacist-managed anticoagulation clinic, in a multidisciplinary setting, is not only safe and effective, but is superior in terms of anticoagulant control and thromboembolic events, with a trend towards lower hemorrhagic events. This is important in the Canadian healthcare context because of the growing service

needs of patients in light of physician shortages, the need for quality improvement in this practice area, and the cost-savings demonstrated herein justify the development of AMSs using this model.

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Table 1: Patient Demographics

	Before / After Analysis N=125	Consecutive Patients N=502	P Value
Age ± (years)	62.9 ± 15.0	59.3 ± 16.9	0.03*
Male (%)	72 (57.6%)	312 (62.2%)	0.35
Indication (n,%)			
Atrial Fibrillation	50 (40.0%)	184 (36.7%)	0.49
Venous Thrombembolism	24 (19.2%)	123 (24.5%)	0.21
Mechanical Valve Replacement	30 (24.0%)	118 (23.5%)	0.90
Other Diagnoses	21 (16.8%)	77 (15.3%)	0.69
PMH:			
No Concurrent Conditions	30 (24.0%)	151 (30.1%)	0.18
CHF	35 (28.0%)	108 (21.5%)	0.12
Liver Disease	10 (8.0%)	35 (7.0%)	0.69
Diabetes	17 (13.6%)	58 (11.6%)	0.53
Hypertension	45 (36.0%)	173 (34.5%)	0.75
Renal Dysfunction	8 (6.4%)	42 (8.4%)	0.47
Malignancy	6 (4.8%)	29 (5.8%)	0.67
Hyperlipidemia	31 (24.8%)	129 (25.7%)	0.84
Thyroid Disease	18 (14.4%)	56 (11.2%)	0.31
Systemic Embolism	39 (31.2%)	117 (23.3%)	0.07
Target INR Range (n,%):			0.75
2.0-3.0	84 (67.2%)	354 (70.5%)	
2.5-3.5	30 (24.0%)	111 (22.1%)	
Other	11 (8.8%)	37 (7.4%)	

*Wilcoxon Test

Table 2: Proportion of Time in INR Range

	N	Prior to referral	During AMS Care	P
Adequacy INR ± 0.5; Mean ± SD (Median, Lower-Upper Quartile)	125	48.8 ± 23.6 (48.7; 32.3-66.2)	66.5 ± 16.3 (69.2; 56.4-78.4)	<0.0001
Adequacy INR ± 0.7 Mean ± SD (Median, Lower-Upper Quartile)	125	65.3 ± 22.3 (66.3; 49.9-83.6)	81.7 ± 12.5 (84.0; 75.2-90.6)	<0.0001
Duration of therapy (mo, Mean ± SD)	125	10.7 ± 10.0; 1341.02 mo	29.3 ± 13.1; 3660.72 mo	<0.0001

Table 3: AMS care- group comparison for adequacy

	N=125	N=502	**P-value**
(INR± 0.5)			0.68
(mean months ± SD)	66.5 ± 16.3	67.2 ± 16.3	
(median, Upper-Lower Q)	69.2, 56.4-78.4	68.9, 57.4-79.2	
(INR± 0.7)			0.73
(mean months ± SD)	81.7 ± 12.5	82.2 ± 13.2	
(median, Upper-Lower Q)	84.0, 75.2-90.6	84.4, 75.9-91.7	

Table 4: ER Visits & Hospitalizations Prior to and During AMS Care

Event type	Prior to AMS Care			During AMS Care			
	N (# pts)	# Events	% event / pt year	N (# pts)	# Events	% event / pt year	P
Bleed - ED	15	21	18.8	9	12	10.8	0.21
Bleed - Hosp	6	7	6.3	5	5	4.5	0.60
Subtotal	17	28	25.1	11	17	15.3	0.25
Clot – ED	22	40	35.8	3	3	2.7	<0.0001
Clot - Hosp	11	15	13.4	1	1	0.9	0.0080
Subtotal	23	55	49.2	4	4	3.6	<0.0001
Other – ED	79	323	289.0	52	137	123.4	<0.0001
Other - Hosp	67	115	102.9	30	48	43.2	0.0007
Subtotal	93	438	391.9	61	185	166.7	<0.0001
Total	98	521	466.2	*66	206	185.6	<0.0001

Table 5: Healthcare System Resource Utilization

	Prior to AMS Care		During AMS Care		Difference	
	ED Hours	Hospitalization Costs	ED Hours	Hospitalization Costs	ED Hours	Hospitalization Costs
Bleeds	176	28,598.15	115	10,549.70	61	18,048.45
Clots	529	106,312	17	2,215.50	512	104,096.50
Other	2217	864,913	992	338,907.80	1,225	526,005.20
Total	2922	999,823.15	1124	351,673.00	1,798	648,150.15