QUALITY IMPROVEMENT REPORT

Oral anticoagulation in a pediatric hospital: impact of a quality improvement initiative on warfarin management strategies

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Background: There are potential risks associated with the use of warfarin in children, particularly as the dosing requirements may decrease as patients get older.

Context: Our facility is a 715-bed freestanding pediatric tertiary care center with a large cardiac surgery center. A significant number of patients receive warfarin for treatment or prophylaxis of thromboembolic events while in hospital.

Key measures for improvement: Initial dose of warfarin and time taken to achieve goal therapeutic international normalized ratio (INR).

Strategies for change: The intervention included: (1) revision of hospital drug formulary so that warfarin dosing was in accordance with the most recent guidelines; (2) warfarin administration restricted to one time of the day (12.00 noon); (3) target therapeutic INR level documented with each warfarin order; and (4) pharmacy computer system mandated that the pharmacist confirmed the target INR, documented the most current INR, and compared the dose with the formulary guidelines. If the warfarin dose was not in accordance with the formulary guidelines, the pharmacist contacted the physician and made dosing recommendations according to the guidelines.

Effects of change: The number of patients with supratherapeutic INR values during the hospital admission was decreased by more than 50% and goal INR values were documented more frequently in the medical record. There was also an increase in subtherapeutic INR values. The intervention had no effect on the time taken to achieve the goal therapeutic INR.

Lessons learned: Instituting changes in a number of aspects of anticoagulation management and incorporating an intensive educational effort across a breadth of healthcare providers can improve anticoagulation management with warfarin in challenging patient populations such as children. Similar methods could possibly improve anticoagulation with other agents such as unfractionated heparin or low molecular weight heparin.

Warfarin has been used for the treatment and prophylaxis of thromboembolic disease for more than 30 years.^{1,2} Even though warfarin has been cited by the United States Pharmacopeia as one of the top 10 medications prone to error, there are many published data detailing the safe and effective use of this drug in adults.³ However, there are considerably fewer data on the use of warfarin in pediatric patients.⁴

OUTLINE OF PROBLEM AND CONTEXT

In general, there are potential risks associated with the use of warfarin in pediatric patients. Warfarin dosing in children is challenging as dosing requirements may decrease as patient age increases.^{5–7} Children younger than 1 year of age require increased warfarin doses, longer times to achieve therapeutic International Normalized Ratios (INRs), more frequent INR testing, and more dose adjustments.⁵ Moreover, the diet of young children may affect the maintenance of therapeutic anticoagulation, as infant formulae contain varying concentrations of vitamin K, a known warfarin antagonist.^{1,4}

Guidelines outlining the management of warfarin in pediatric and adult patients have been published as a supplement to *Chest*.¹ However, many of the indications for which children are treated do not have detailed treatment guidelines and may be controversial, such as the Fontan procedure or coronary thrombi and Kawasaki's disease.^{8,9} In addition, most pediatricians have limited experience in managing patients who require warfarin therapy.

A significant number of our patients are adults (>18 years of age), which can present additional challenges to pediatricians. This is a result of advances in the surgical and medical management of patients with congenital heart disease. Currently, 85% of children born with congenital heart defects survive into adult life.¹⁰ In the US alone, there are one million patients with corrected, palliated, or uncorrected congenital heart disease, and this cohort is growing at an annual rate of 5%.¹¹ By 2010 there will be as many adults as children who will be having surgery for congenital heart disease in the UK; there is therefore a national need to define provisions for this group of patients.^{12,13} At present the management of these adult patients occurs at our pediatric institution.

ASSESSMENT OF PROBLEM

Due to the difficulty of managing warfarin in pediatric patients and the propensity for undesirable outcomes (bleeding), we performed a retrospective analysis of all patients treated with warfarin at our institution from 1 January 2002 to 30 June 2002. Our facility is a 715-bed freestanding tertiary pediatric center with a large center for cardiac surgery. Due to the large cardiac surgical program, a significant number of patients receive warfarin for treatment or prophylaxis of thromboembolic events while in hospital.

Abbreviations: INR, international normalized ratio; QI, quality improvement

Data collected included patient name, age, cardiac defect, warfarin dosing, time to achieve therapeutic INR, side effects, dosing trends, efficacy of anticoagulation using INR data, supratherapeutic and subtherapeutic INR levels, and adverse events associated with warfarin.

After the data collection and analysis, a survey was given to all physicians, nurses, and pharmacists who provide care for this subset of patients. The questions were centered on two patient cases and focused on the following topics:

- appropriate goal INR range;
- appropriate initial dosing of warfarin;
- appropriate monitoring of INR value;
- dietary concerns with warfarin therapy;
- discharge education;
- drug interactions; and
- references concerning management of warfarin therapy.

STRATEGY FOR CHANGE

A comprehensive review of the results of the retrospective analysis and survey was presented to all of the pertinent healthcare providers. As a result of the analyses and presentation, the following quality improvement (QI) interventions were implemented as practice modifications in September 2003:

- The hospital drug formulary was revised so that warfarin dosing was in accordance with the most recent guidelines published in *Chest*.¹
- Warfarin administration was restricted to one time of the day (12.00 noon).
- The target therapeutic INR level was documented with each warfarin order.
- A prompt within the pharmacy computer system mandated that the pharmacist (1) confirmed the target INR, (2) documented the most current INR, and (3) compared the dose with the formulary guidelines. If the warfarin dose was not in accordance with the formulary guidelines, the pharmacist would contact the physician and make dosing recommendations according to guidelines.

Data were collected prospectively from 1 December 2003 to 30 May 2004 and compared with the data collected before the intervention. For analysis, the cohort was divided into two groups. The pre-intervention group comprised patients who were admitted before implementation of the QI interventions and the post-intervention group consisted of patients who were admitted after implementation of the interventions. Unless cited differently, values are expressed as mean (SD). Each patient admission was analyzed as a separate event. An

association between the intervention and the outcome was assessed using binary logistic regression with robust standard errors adjusted for clustering on person. Odds ratios and robust confidence intervals were also included. This analysis was done using Stata 8.2. Statistical significance is defined as $p < 0.05$.

EFFECTS OF CHANGE

Study cohort

Fifty eight patients who had 71 hospital admissions received warfarin during the period of review. Their median age was 18 years (range 1–46). A total of 361 inpatient warfarin days were documented. The indications for warfarin anticoagulant therapy are shown in table 1. No patient had any bleeding episodes that were attributed to warfarin therapy and there were no deaths attributable to the treatment.

Pre-intervention group

The pre-intervention group consisted of 25 patients who had a total of 31 admissions during the study period, with a total of 151 inpatient warfarin days. Their median age was 18 years (range 3–32). At the time of hospital admission, 18/31 (58%) were being treated with warfarin and warfarin therapy was initiated during the admission in 13 patients.

ACCP guidelines for initiation of warfarin therapy were followed in 5/13 (39%) patients. Patients ≤ 18 years of age were analyzed separately from those aged >18 years in order to characterize accurately the warfarin dosing schemes. The mean (SD) dose for patients ≤ 18 years was 0.075 (0.03) mg/kg, and 5.45 (1.6) mg for those aged >18 years. No patients aged ≤ 18 years required the maximum initial dose of 5 mg. The mean (SD) time to achieve a therapeutic goal INR was 4.25 (1.4) days in patients newly initiated on warfarin.

Post-intervention group

The post-intervention group consisted of 33 patients who had a total of 40 admissions during the study period, with a total of 210 inpatient warfarin days documented. The median age was 18 years (range 1–46). At the time of hospital admission, 26/40 (65%) patients were being treated with warfarin. Warfarin therapy was initiated during the admission in 14 patients.

ACCP guidelines were followed for the initiation of warfarin therapy in 5/14 (36%) patients. Patients ≤ 18 years of age were analyzed separately from those aged >18 years of age in order to characterize accurately the warfarin dosing schemes. The mean (SD) starting dose for patients ≤ 18 years of age was 0.18 (0.03) mg/kg compared with 0.075 (0.03) mg/kg in the pre-intervention group ($p = 0.02$). Three patients received the maximum initial dose of 5 mg. The mean (SD) starting dose for patients >18 years of age was 6.1 (2.2) mg. One patient received a 10 mg dose, which exceeds the upper limit of recommended dosing.

Patients newly initiated on warfarin therapy achieved a therapeutic goal INR in 4.3 (1.4) days compared with 4.25 (2.6) days in the pre-intervention group ($p = 0.98$). Other variables related to dosing are summarised in table 2.

LESSONS LEARNED

There are different strategies by which healthcare centers can provide optimal management of anticoagulation with warfarin. One such strategy is the use of a dedicated pharmacy service that manages oral anticoagulation. This strategy has been associated with a decrease in healthcare costs and a decrease in warfarin related morbidities in inpatient and outpatient settings.^{6, 14–17}

However, in order to address issues with the management of warfarin in our center, we chose an alternative strategy that involved an educational initiative for all healthcare

Table 1 Indications for warfarin therapy

Indications	Pre-intervention (n = 25)	Post-intervention (n = 33)
Atrial fibrillation/flutter	9	11
Fontan operation	5	6
Pulmonary hypertension	5	6
Mitral valve replacement	1	3
Aortic valve replacement	1	3
Intracardiac thrombus	2	–
Cerebral vascular accident	2	–
Dilated cardiomyopathy	–	1
Coronary artery thrombus	–	1
Homograft stenosis	–	1
Hypercoagulable state	–	1

Table 2 Data on warfarin therapy (patient admissions)

	Pre-intervention (n = 31)	Post-intervention (n = 40)	p value	Odds ratio	95% CI
In-hospital					
Goal INR documented in chart	4/31 (13%)	34/40 (85%)	<0.0001	38.2	9.72 to 150.5
Therapeutic INR level	17/29 (58%)*	22/37 (59%)†	0.379	0.62	0.21 to 1.79
Supratherapeutic INR level	12/29 (41%)*	7/37 (19%)‡	0.039	0.32	0.11 to 0.95
Discharge					
Therapeutic INR level	8/26 (31%)‡	15/33 (45%)§	0.287	1.78	0.62 to 5.12
Supratherapeutic INR level	11/26 (42%)‡	2/33 (6%)§	0.043	0.22	0.05 to 0.95
Subtherapeutic INR level	7/26 (27%)‡	16/33 (48%)§	0.11	1.03	0.37 to 2.89

*INR level not known in two patients.

†INR level not known in three patients.

‡INR level not known in five patients on day of discharge.

§INR level not known in seven patients on day of discharge.

providers. Our goal was to achieve improved outcomes by improving the baseline knowledge of anticoagulation management in each healthcare provider. It was felt that the best outcomes would occur if every provider at our institution had baseline knowledge of anticoagulation with warfarin. As an academic hospital whose mission is to train future healthcare providers, it is very important that we enhance the education of trainees with an intensive educational effort. This may not happen with a separate anticoagulation service.

A survey and retrospective analysis identified knowledge deficits and helped to direct the presentation. This presentation proved useful for providing awareness of current practices of warfarin management, the need for a management strategy, and allowed for education of available resources for warfarin management.

The institution of a warfarin dosing restriction to noon prevented patients from receiving two warfarin doses within a 24 hour period, which occasionally occurred before the study. Thus, supratherapeutic INR levels from multiple doses were prevented. The restriction to noon may have improved the clinical pertinence of INR data, as INR values are consistently drawn with morning laboratory data, resulting in similar lengths of time between warfarin dosing and laboratory evaluation for all patients.

We believe that each intervention was important for staff education and sustainability of the QI initiative. In addition, we believe that the initiative would have been less successful had there only been an educational component or an intervention component, as all of the interventions were related to educating prescribers. For example, an inappropriate dose would warrant a call by the pharmacist to educate the prescriber on the appropriate dosing, as outlined in the hospital formulary. Prescribers were therefore educated on the QI initiative because of the interventions that were put in place. The initial education component is sustained because of the interventions put in place by the initiative. Both initial education and interventions were necessary to achieve results.

The number of patients with supratherapeutic INR values during the hospital admission was decreased by more than 50%. This may be due in part to appropriate initial dosing of warfarin. Anecdotally, in the pre-intervention group the authors noticed a trend of cautiousness when initially dosing a patient on warfarin, only to have more aggressive dosing later when patients did not achieve goal INR in a satisfactory time period. This may have been a cause of increased goal INR values. The goal INR values were also documented more frequently in the medical records of patients in the post-intervention group, which may have contributed to an increased awareness of patient INR values and improved outcomes.

In addition to an increase in therapeutic INR values and a significant decrease in supratherapeutic INR values on discharge, there was also an increase in subtherapeutic INR values. While subtherapeutic values are not ideal, there are several explanations. We hypothesize that increased awareness of goal INR values may have led to more caution regarding the adverse events associated with increased INR values, thus resulting in subtherapeutic INR levels. Subtherapeutic INR values were often due to patients having 24–48 hour admissions for reversal of anticoagulation prior to procedures. After the procedure the patients were restarted on warfarin doses that had previously rendered therapeutic INR values and discharged before obtaining a therapeutic INR in the hospital. This may also have accounted for those patients who did not have INR values drawn during admission. Finally, the time to achieve goal INR for patients newly started on warfarin therapy was similar in both groups. Patients reached the goal value in the hospital after being started on warfarin, but may have had a normal fluctuation in the INR value to a subtherapeutic level before discharge. While patients are in hospital, the option of starting injectable anticoagulants is feasible so subtherapeutic values and the issue of thrombus formation were not of great concern for our patient population.

There are several limitations to our approach to the management of warfarin therapy. The pharmacists were only able to evaluate new orders for warfarin. A patient could therefore have been on a consistent dose of warfarin and the pharmacist would not have known to evaluate the INR and dose daily. The outcomes presented could perhaps be improved if a pharmacist evaluated every dose of warfarin for each patient. Since this initial QI intervention, each dose of warfarin is evaluated and recommended by a pharmacist. Post-intervention results will most likely improve with continued active use of the initiative.

Key messages

- Instituting changes in a number of aspects of anticoagulation management and incorporating an intensive educational effort across a breadth of healthcare providers can improve anticoagulation management with warfarin in challenging patient populations such as children.
- Similar methods could possibly improve anticoagulation with other agents such as unfractionated heparin or low molecular weight heparin.

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