Implementation and Evaluation of a Pharmacist-Assisted Warfarin Dosing Program

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ABSTRACT

The purpose of this study was to implement a Pharmacy-Assisted Warfarin Dosing (PAWD) Pilot Program and assess its effects on efficiency, effectiveness, and safety during warfarin anticoagulation. A protocol was developed based on institutional anticoagulation guidelines. Pharmacists on three nursing units anticoagulated patients by protocol upon physician request (PAWD group, n=24). All warfarin orders were written by a pharmacist in accordance with hospital policies. The study group was compared with a baseline sample of patients started on warfarin therapy by physicians (Control group, n=34).

The number of patients achieving the target INR by day 5 (Control - 41.1 % and PAWD - 32 %) was not significantly different among the 2 groups. The PAWD program resulted in significant improvements to the number of warfarin doses administered on time (99.1 %) compared to the Control group (46.2 %). Both groups had a low incidence of bleeding (Control - 6.06 % and PAWD - 8 %) and thromboembolic events (Control - 3.03 % and PAWD - 0 %). Overall, the PAWD program resulted in equally effective and safe anticoagulation of patients and improved compliance with timely administration of doses.

Key words: anticoagulation, dosing, guidelines, prescribing, program, warfarin

RÉSUMÉ

Le but de cette étude était de mettre sur pied un programme pilote de dosage de la warfarine assistée par le pharmacien (DWAP) et d'en évaluer sur l'efficience, l'efficacité et la sécurité dans le cadre d'une anticoagulothérapie à la warfarine. Un protocole a été élaboré, à partir des lignes directrices institutionelles sur l'anticoagulothérapie. Les pharmaciens de trois unités de soins ont amorcé une anticoagulothérapie à des patients selon le protocole établi, à la demande du médecin (groupe DWAP, N=24). Toutes les demandes de warfarine ont été écrites par un pharmacien, selon les politiques de l'hôpital. Le groupe expérimental a été comparé à un groupe de patients chez qui l'anticoagulothérapie a été amorcée par des médecins (groupe témoin; N = 34).

Le nombre de patients qui a atteint le RIN cible au jour 5 (témoins : 41,1 % et DWAP : 32 %) n'était pas significativement différent entre les deux groupes. Le programme DWAP a entraîné des améliorations notables du nombre de doses de warfarine administrées selon l'horaire établi (99,1 %), comparativement au groupe témoin (46,2 %). L'incidence des saignements (témoins : 6,06 % et DWAP : 8 %) et des thromboembolies (témoins : 3,03 % et DWAP : 0 %) était faible dans les deux groupes. Dans l'ensemble, le programme DWAP a permis d'administrer d'une façon aussi sûre et efficace qu'avec la méthode classique l'anticoagulothérapie et de respecter davantage l'horaire d'administration des doses.

Mots clés : anticoagulothérapie, dosage, lignes directrices, prescription, programme, warfarine

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INTRODUCTION

Formulating safe and effective warfarin doses is difficult, especially when initiating anticoagulation therapy. Due to the many variables which can affect patient response, the potential for dosing errors exists. Differences in prescriber knowledge and experience result in widely swinging intensities of anticoagulation. Therapy is further complicated in an acute care hospital where different physicians with varying approaches to anticoagulation may be responsible for ordering consecutive warfarin doses for a single patient.

Proactive participation of pharmacists may help improve anticoagulation practices, due to their knowledge of warfarin therapeutics, pharmacokinetics, and drug interactions. One method of more actively involving pharmacists in influencing prescribing patterns is the

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concept of "dependent prescribing under protocol."[1] Under such a system, a protocol consisting of a "set of guidelines, standards, policies or steps" is prepared by physicians in collaboration with pharmacists for use in the process of prescribing.[2,3] Upon the request of the physician, the pharmacist is authorized to determine dgsing regimens for patients according to the approved protocol.

The advantages of applying such a program to warfarin therapy were recognized at The Toronto Hospital. "Pharmacist-Assisted Warfarin Dosing (PAWD)", utilizing approved institutional anticoagulation guidelines, would ensure a more consistent approach to anticoagulation. By demonstrating to the medical housestaff the use of an efficient, safe, and effective method of anticoagulation, pharmacists would proactively contribute to housestaff education. The consistent availability of pharmacists on the wards would allow laboratory results to be interpreted as soon as they are available, thus ensuring that medication orders are written prior to the standard 18:00 hour administration time.

The purpose of this study was to: 1) implement a PAWD pilot program on cardiology and vascular surgery units; 2) evaluate the impact of this program on efficacy, efficiency, and safety in achieving designated therapeutic levels of anticoagulation compared to physician directed anticoagulation; and 3) evaluate the impact on the efficiency of ordering warfarin doses.

METHODS

A) Pilot Program Implementation

The initial pilot project proposal was approved by The Toronto Hospital (TTH) Residency Advisory Committee and the Pharmacy and Therapeutics Committee. Although the project did not require approval of the TTH Committee for Research on Human Subjects, it was approved in principle by the committee.

A protocol was developed incorporating institutional anticoagulation guidelines prepared by the Haematologist-in-Charge and The Department of Pharmacy Services (Figure 1) for use on cardiology and vascular surgery units.[4-7] An educational, self-learning package was developed to review the principles of warfarin therapy and to familiarize the eight participating pharmacists with

Target INR 2.5

Thrombosis, thromboemboli and excess clotting associated with deep vein thrombosis; venous thromboembolism; bioprosthetic heart valves

First Day		Second Day		Third Day		Fourth Day, and onwards	
INR	Dose (mg)	INR	Dose (mg)	INR	Dose (mg)	INR	Dose (mg)
< 1.3	10	< 1.3	10	< 1.6	10	< 1.8	10
1.3 - 1.5	5	1.3 - 1.5	5	1.6 - 1.8	7.5	1.8 - 2.1	7.5
> 1.5	nil	> 1.5	nil	1.81 - 2.1	5	2.11 - 2.4	5
				2.11 - 2.4	2.5	2.41 - 2.5	2.5
				2.41 - 2.7	1.25	2.51 - 2.7	1.25
				> 2.7	nil	> 2.7	nil

Target INR 3.5

Thrombosis or thromboemboli and excess clotting associated with mechanical heart valves and intravascular devices; arterial thromboembolism.

First Day		Second Day		Third Day		Fourth Day, and onwards	
INR	Dose (mg)	INR	Dose (mg)	INR	Dose (mg)	INR	Dose (mg)
< 1.3	10	< 1.3	10	< 1.7	10	< 2	10
1.3 - 1.5	5	1.3 - 1.5	5	1.7 - 2.2	7.5	2.0 - 2.5	7.5
> 1.5	nil	> 1.5	nil	2.21 - 2.7	5	2.51 - 3.0	5
				2.71 - 3.2	2.5	3.01 - 3.4	2.5
				3.21 - 3.6	1.25	3.41 - 3.7	1.25
				> 3.6	nil	> 3.7	nil

INR increases too early after starting warfarin or INR increases too much after starting warfarin	INR fails to increase or INR increases too little according to the expected dose response relation
If INR increases by 0.5 after any dose: Give only half dose recommended for INR. If INR increases by > 1 after any single dose: 1) Check for liver disease, drug interference, poor nutrition, vitamin K intake, diet, diarrhea, etc. 2) Give only one quarter (25%) of the dose.	If INR not > 1.3 after 4 consecutive doses of 10 mg: 1) Check for ingestion of Vitamin K e.g., nutrition supplements, seaweed or ethnic food, kale, proprietary vitamins, etc. 2) Crush tablet, dissolve in water and watch patient swallow medication with a juice chaser. If still no increase in INR after 24-48 hours: Use twice the dose recommended, but check INR carefully. If INR stops increasing after initial satisfactory response: Check diet, drug, and compliance again.

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Figure 1. Anticoagulation Guidelines: Warfarin Therapy

protocol procedures.[8-12] A series of cases with questions were devised to assess each pharmacist's knowledge and proficiency in using the protocol. The program was promoted through physician and nursing inservices. The pilot program was offered for a 6-week period between March 21 and May 1, 1994.

Seven days a week during the study period, the pharmacists responsible for the participating patients initiated the protocol after receiving a physician order requesting PAWD with a specified target therapeutic INR. The pharmacist assessed the patient's status by recording the necessary information on a monitoring profile. If, in the pharmacist's clinical judgement, the patient required a dose outside of the approved protocol, the responsible physician or anticoagulation service was contacted. Warfarin doses were written per institutional policy as verbal orders from the initiating physician and required a cosignature within 24 hours. Physicians were offered the option of withdrawing their patients from the program at any time. If the patient required reversal of anticoagulation, the pharmacist made recommendations regarding the reversal of anticoagulation to the house officer or designate. The pharmacy staff were in active consultation with the Haematologist-in-Charge and the Pharmacy Clinical Coordinator regarding exceptional patients who required therapy outside of the protocol.

B) Evaluation of the Pilot Program

The program was evaluated through the comparison of a control group of patients to those receiving the PAWD program. Any patients being initiated on warfarin therapy or being reinitiated on warfarin therapy following vitamin K reversal were included in the study. Patients receiving less than three doses of warfarin before discharge or already receiving maintenance therapy were excluded. Patients concurrently receiving medications which interacted with warfarin were not excluded. Data for the control group were collected from cardiology and cardiovascular surgery patients enrolled during a 4-week period prior to program implementation according to the previously stated inclusion and exclusion criteria. Control data from vascular surgery patients could not be collected since this group was not enrolled in the PAWD study until after the baseline assessment was undertaken.

Clinical notes and laboratory values were recorded on pharmacy patient profiles. Baseline data consisted of patient gender, age, number of disease states, presence of congestive heart failure, liver dysfunction, number of regularly scheduled medications, and medications interacting with warfarin. The number of medications interacting with warfarin that were discontinued and warfarin doses changed due to pharmacists' suggestions were also recorded.

Primary outcomes consisted of the number of patients who achieved therapeutic INR range by day 5, the number of doses prescribed and received on time, and the number of bleeding episodes or thromboembolic events patients experienced. Secondary therapeutic outcomes consisted of the number of days of warfarin therapy, days to obtain target INR, days INR was within target range, days INR was under range, and days INR was over range. Bleeding was classified by severity. Major bleeding was defined as a hemorrhage associated with a decrease of 20 g/L of hemoglobin or more, requiring blood transfusion, or involving intracranial, intraocular, intraarticular or retroperitoneal bleeding. Minor bleeding was defined as bleeding not meeting the above criteria. Other adverse event criteria included INR values greater than 4 per patient, doses of vitamin K per patient, and average dose of vitamin K.

Due to the non-random selection of patients in the pilot program group, non-parametric tests for two independent groups of data, Fischer's Exact Test, Chi-Square with Yeat's correction (α=0.05), and the Mann Whitney U Test were used where appropriate.

RESULTS

Data for 46 patients on warfarin therapy in the control group were collected. Based on previously stated criteria, 12 patients were excluded (Table I). On floors being offered the PAWD program, 17 patients were excluded from the total of 41 eligible patients. One patient in the PAWD program was initiated on warfarin therapy twice, bringing the total number of analyzable results to 25.

Baseline characteristics of both groups were similar (Table II). Patients in the PAWD group had a higher incidence of congestive heart failure (32% versus 20.6 % in control) and were receiving more medications per patient on average (5.2 versus 4.3 in control). None of these differences, however, were statistically significant.

The indications for warfarin therapy are listed in Table III. Of the indications considered, only 2 differed significantly. Significantly more patients were being anticoagulated for deep vein thrombosis (28%) in the

Table I. Patients Excluded

Variable	Control	Pharmacist Assisted Warfarin Dosing
Total Number of Patients Reviewed	**46**	**41**
New Start (<3 Days of Warfarin)	9	2
Maintenence Therapy	1	12
PAWD Declined	Not Applicable	3
Data Lost to Follow-up	2	0
Total Number of Patients Excluded	**12**	**17**

Table II. Patient Demographics

Variable	Control (n = 34) Result ± SD	Pharmacist Assisted Warfarin Dosing (n = 25) Result ± SD
Gender (male)	47.1 %	72.0 %
Age (years)	58.7 ± 15.6	61.5 ± 13.1
Diseases States per Patient	3.4 ± 1.7	3.6 ± 1.6
Congestive Heart Failure	20.6 %	32.0 %
Liver Dysfunction	0.0 %	0.0 %
Medications per Patient	4.3 ± 2.6	5.2 ± 2.9
Medications Interacting with Warfarin per Patient*	1.0 ± 1.1	1.1 ± 0.9
Interacting Medications Discontinued per Pharmacist Suggestion	25.8 %	28.6 %

* Prior to pharmacist intervention.

Table III. Indications for Warfarin Therapy

Variable	Control (n = 34)	Pharmacist Assisted Warfarin Dosing (n = 25)
Deep Vein Thrombosis (prophylaxis)	0.0 %	4.0 %
Deep Vein Thrombosis (treatment)	2.9 %	28.0 %*
Pulmonary Embolism (treatment)	0.0 %	8.0 %
Tissue Heart Valve	11.8 %	0 %
Myocardial Infarction	2.9 %	20.0 %
Atrial fibrillation	17.6 %	24.0 %
Recurrent Systemic Embolism	5.9 %	8.0 %
Cardiomyopathy	2.9 %	8.0 %
Valve Repair with Ring	17.6 %	0.0 %
Mechanical Prosthetic Valve	57.6 %	8.0 %**
Other	2.9 %	4.0 %

* Statistically significant using Fischer's Exact Test (p = 0.017)
** Statistically significant using Chi-square with Yeat's correction (α = 0.05)†.

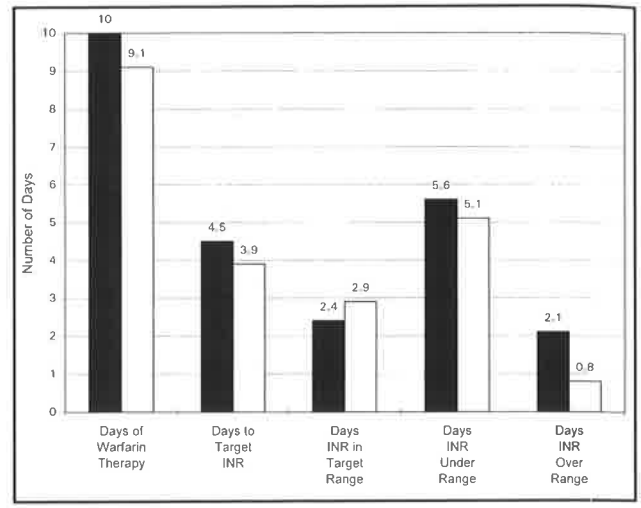

Figure 2. Primary Outcome Variables

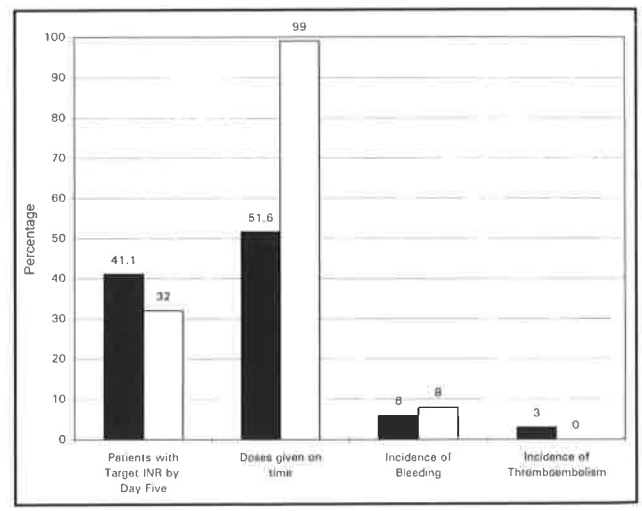

Figure 3. Secondary Therapeutic Outcome Measures

PAWD group compared to the control group (2.9%). In addition, the PAWD program also had significantly fewer patients receiving anticoagulation for mechanical prosthetic valves (8%).

Analysis of primary outcome variables (Figure 2) did not show significant differences in the percentages of patients achieving the target INR by day 5 in the control (41.1%) or PAWD (32%) groups. However, the warfarin prescribing process was significantly improved in the PAWD program, with a significantly higher percentage of doses received on time in the PAWD group (99.1%)† compared to the control group (46.2%). Adverse effects were infrequent and did not differ significantly between the two groups.

No differefces were observed between the groups in secondary therapeutic outcome measures (Figure 3). Patients in the PAWD program appeared to have fewer days of warfarin therapy per patient (9.1) compared to the control group (10). Those in the PAWD program were also less likely to overshoot the target within the first 5 days (24% compared to 32.4% the control group.) No statistically significant differences were seen in the number of days within the target INR range per patient (control - 2.4, PAWD - 2.9) or t`e number of days under the target (control - 5.6, PAWD - 5.1). The number of days over the target INR in the control group was 2.1. The average time to target therapeutic INR was not significantly different for the patients in the PAWD program (3.9 days) compared to the control (4.5 days).

In terms of the secondary process outcome measures, the PAWD program proved to have a positive impact on the time orders were written, with 99.1%† of warfarin

† Chi-Square with Yeat's correction (α=0.05)

Table IV. Adverse Events

Variable	Control (n = 34)	Pharmacist Assisted Warfarin Dosing (n = 25)
Major Bleeds	0.0 %	0.0 %
Minor Bleeds	6.1 % (2/34)	8.0 % (2/25)
INR values > 4 per patient	0.5	0.083*
Doses of Vitamin K per patient	0.2	0.0
Average Dose of Vitamin K	1.5 mg	0.0 mg
Thromboembolic Events	3.0 % (1/34)	0.0 %

* Statistically significant using Mann Whitney U Test (p = 0.0059)

orders being received prior to the standard 18:00hr administration time. The percentage of orders being received prior to 18:00hr were 46.2% control group. Doses dispensed from the night cupboard (after 21:00hr when the pharmacy is closed) in the PAWD group (0%) were significantly reduced compared to the control (16.8%) group.

There were no significant differences in bleeding episodes Minor bleeding occurred in 2 patients in the control group. One patient suffered hematuria, while the INR was subtherapeutic. A second patient experienced bruising associated with a therapeutic INR. Two patients in the PAWD program also suffered minor bleeding. The first patient, who was concurrently receiving a heparin infusion, experienced a nosebleed while the INR value was subtherapeutic and the aPTT was greater than 150 seconds. The second patient with a therapeutic INR bled after biting his cheek. Fewer doses of vitamin K were administered to the PAWD group than the control. Thromboembolic events occurred only in the control group, with one patient experiencing a mural thrombus documented by transesophageal echocardiography (TEE) and possible pulmonary embolus. The pulmonary embolus was not confirmed by ventilation-perfusion scan.

DISCUSSION

Patients anticoagulated through the PAWD program did not show a statistically significant difference in the number of patients attaining the target INR by day 5 compared to the physician directed control group. This demonstrates that pharmacists were able to determine effective anticoagulation regimens for patients through the use of a dosing protocol incorporating institutional guidelines. These results can have a significant impact on relieving the workload of housestaff while providing equally effective anticoagulation practices.

Patients enrolled in the PAWD program did not show a statistically significant difference in the percentage of patients experiencing adverse events compared to the control group. This further demonstrates that the PAWD program was a safe means of anticoagulating patients. In addition, significantly more patients receiving the PAWD program were prescribed and administered warfarin doses on time than patients in the control group. As a result, the PAWD program resulted in greater efficiency in processing of warfarin orders by the pharmacy staff and administration of doses by the nursing staff.

Statistically significant differences were not observed in the majority of secondary therapeutic outcome variables. The number of days the INR was over the target range was significantly lower in the PAWD patients than the control patients. This may indicate that physicians were more likely to prescribe larger warfarin doses than necessary for patients. However, the higher INR values could also be attributed to more aggressive dosing practices used for numerous patients with higher target INR's (e.g., mechanical heart valves) seen in the control group.

Secondary adverse effect measures were consistent with primary outcomes. No differences were observed when bleeding was classified by severity, and the use of vitamin K was low in all groups of patients. Consistent with the lower incidence of INR values above the therapeutic range, significantly fewer PAWD patients had INR values greater than 4 and no vitamin K was used in this group of patients.

It became obvious during the study that, although the warfarin anticoagulation guidelines provided a useful means to initiate warfarin therapy during the first 4 or 5 days, response to warfarin and patient trends became a more important consideration in determining subsequent doses. Pharmacists and medical staff commented that the guidelines were less successful in maintaining target INRs, although this observation was not universal and not the purpose for which the guidelines were developed.

Despite increased use of the guidelines, statistically significant improvements in the number of patients reaching the target INR by day 5 were not observed. Day 5 was chosen as a standard since it has been reported in the literature that the majority of patients should be adequately anticoagulated within this time frame.[12] Increased use of the warfarin dosing guidelines showed trends toward improved anticoagulation practices, although statistically significant differences were not detected in this study. Future studies involving larger study populations are needed to more thoroughly assess improvements to anticoagulation practices.

Additional study is also required to address application to specific subpopulations. The PAWD group was smaller than anticipated due to the late decision to not include cardiovascular surgery patients at the request of hospital staff in these areas. Future studies should be performed to assess the impact of the PAWD program on cardiovascular surgery patients. More data are also

needed for vascular surgery patients. The unanticipated late inclusion of these patients at the request of the Division Head of Vascular Surgery prevented the collection of baseline data. Nevertheless, the vascular surgeons expressed the belief that the pharmacists were significantly more efficient in anticoagulating this population of patients than the interns and residents.

Certain challenges were encountered which had to be addressed prior to and during the implementation of the pilot program. The first major issue which emerged was that of implementation of dosing by protocol at a major teaching institution. Similar programs have been implemented in Canada and the United States in community hospitals, where teaching was not a major focus.[14] A concern was expressed by members of the Pharmacy and Therapeutics Committee that housestaff would be out of touch with the anticoagulation status of their patients and not learn the proper technique for anticoagulation. This concern was addressed by requiring cosignature of all orders written by pharmacists for the program. In addition, doses which were determined through clinical judgement and experience, rather than strict adherence to the protocol had to be discussed with the housestaff prior to writing the order. Clear documentation explaining the rationale for such doses was also indicated in the chart, as well as documentation of any other complicating factors which had to be considered. Thus, utilization of the guidelines in the PAWD program demonstrated to housestaff a reasonable and consistent approach to anticoagulating individual patients.

The second issue which needed to be addressed was the ultimate responsibility for the patient. Under current standards of practice, pharmacists are legally responsible for the well being of patients, with regards to drug therapy, and can also be liable in a case of malpractice. Everyday pharmacists routinely make recommendations regarding dosing of all drugs including those with a narrow therapeutic index. All activities performed by pharmacists in the PAWD program were consistent with current standards of practice. By treating orders written accordang to protocol as verbal orders requiring cosignature, and requiring physician approval of orders written outside of the protocol, a double-check system was in place. This was analogous to the current system of requiring all physician orders to be reviewed by pharmacists. As demonstrated by this project, patients were anticoagulated as safely by pharmacists through the PAWD program as by physicians. In fact, if one examines the data further, the one incidence of minor bleeding in the PAWD group was clearly related to excessive anticoagulation with heparin therapy while the other was associated with the mishap of the patient biting his cheek.

A pharmacy issue that needed to be addressed was the feasibility of providing such a program given existing staff and resources. Initially, concerns were raised regarding the significant time commitment that was necessary for pharmacists to adequately profile patients who were being anticoagulated in this program. However, detailed profiling of patients was advantageous not only for the PAWD program but for the routine provision of pharmaceutical care as well. Prioritization was necessary to continue to provide all expected pharmacy services. Profiles which could not be completed during times of light staff coverage such as evenings or on weekends were completed the following day. Similar time issue concerns were raised regarding chart documentation. Documentation, however, was an essential part of the program to inform other health professionals of the pharmacist's activities, and for legal reasons. A streamlined documentation method was developed to assist in the process. Efficiency in documentation improved as more patients were entered into the program but continued to be a difficult issue for pharmacists throughout the study.

Finally, the issues of continuing education and quality assurance were considered but need to be more fully addressed for the future continuation of the PAWD program. Certification of pharmacists was addressed through the development of a training package and test. A more formalized recertification process would be necessary to ensure the continued competence of pharmacists who provide such a service. All pharmacists activities were audited concurrently during the pilot program. To ensure the ongoing quality of the PAWD program, a regular review mechanism is currently being developed.

The implementation and evaluation of a program which provides a mechanism for pharmacists to dose drug therapy for patients by protocol has implications for the future direction of pharmacy practice. Increasingly, various health care professionals other than physicians have been delegated the act or given the responsibility to prescribe. Recent examples in the U.S. and Canada include pharmacy practitioners, nursing practitioners, and midwives.[11,15] Due to their inherent knowledge and training, pharmacists would appear to be an appropriate choice for transferring responsibility for determining effective drug regimens for patients. The results of this project suggest that pharmacists are able to anticoagulate patients with similar efficacy and safety as physicians, as well as increased efficiency. In addition, the delegation of greater responsibility to pharmacists would be a natural progression of a multi-disciplinary approach to health care. In a major teaching institution such as The Toronto Hospital, the intent would not be to deny housestaff the opportunity of anticoagulating their own patients. Rather, the commitment of pharmacists to educating others on rational drug regimens would be increased.

In conclusion, despite positive trends, the PAWD program did not show a significant difference in therapeutic outcome measures or adverse effects compared to the control group. Significant improvements were observed, however, in process outcome measures of patients in the PAWD program compared to the control group. Through the PAWD program, pharmacists appeared to anticoagulate patients with equal effectiveness and safety compared to physicians. Through increased awareness and use of institutional anticoagulation guidelines and increased involvement of pharmacists, the PAWD program showed promise in improving effective anticoagulation of patients. As a result, implementation of the PAWD program has occurred in the cardiology units at The Toronto Hospital and extensions of the program are currently being evaluated in other patient care areas such as orthopedics.

REFERENCES

1. Copeland GP, Apgar DA. The pharmacist practitioner training program. *Drug Intell Clin Pharm* 1980;14:114-9.
2. Covington, TR. Toward rational approach to the issue of prescribing authority for pharmacists. *Drug Intell Clin Pharm* 1983;17:660-6.
3. Martin JK, Norwood MB. Pharmacist management of antiemetic therapy under protocol in an oncology clinic. *Am J Hosp Pharm* 1988;45:1322-8.
4. Fennerty A, Dolben J, Thomas P, et al. Flexible induction dose regimen for warfarin and prediction of maintenance dose. *Br Med J* 1984;228:1268-70.
5. Holford, NHG. Clinical pharmacokinetics and pharmacodynamics of warfarin - understanding the dose - effect relationship. *Clin Pharmacokin* 1986;11:483-504.
6. Shetty HGM, Fennerty AG, Routledge PA. Clinical pharmacokinetic considerations in the control of oral anticoagulant therapy. *Clin Pharmacokin* 1989;16:238-53.
7. Glynn MFX, The Department of Pharmacy Services. Anticoagulation guidelines: warfarin therapy. The Toronto Hospital Formulary. Toronto: The Toronto Hospital; 1996:224-5.
8. Hirsh J, Dalen JE, Deykin JE, et al. Oral Anticoagulants: mechanism of action, clinical effectiveness and optimal therapeutic range. *Chest* 1992;102 (Suppl 4): 312S-26S.
9. Anonymous. Chapter 8: Principles of oral anticoagulant drug interactions. In: Hansten PD, Horn JR, eds. Drug Interactions, and Updates. Philadelphia: Lea & Febiger, 1993:57-61.
10. Buckely NA, Dawson AH. Drug Interactions with warfarin. *Med J Aust* 1992;157:479-83.
11. Landefeld CS, Beyth RJ. Anticoagulant-related bleeding: clinical epidemiology, prediction and prevention. *Am J Med* 1993;95:315-27.
12. Brigden M. Oral anticoagulant therapy - New indications and an improved method of monitoring. *Postgrad Med* 1992;91:285-96.
13. Turpie AGG, Gent M, Laupacis A, et al. A comparison of aspirin with placebo in patients treated with warfarin after heart valve replacement. *N Engl J Med* 1993;329:524-9.
14. Rivey MP, Wood RD, Allington DR, et al. Pharmacy-managed protocol for warfarin use in orthopedic surgery patients. *Am J Health-Syst Pharm* 1995;52:1310-6.
15. Anonymous. Statutes of Ontario - Chapter 18. In: Regulated Health Professions Act,Toronto: The Queen's Printer for Ontario, 1994:9.