COST SAVINGS AND EFFECTIVENESS OF OUTPATIENT TREATMENT WITH LOW MOLECULAR WEIGHT HEPARIN OF DEEP VEIN THROMBOSIS IN A COMMUNITY HOSPITAL

Ming Lee B. Sc. Phm ¹, David Pao B. Sc. Phm², Tom Hsu B. Sc. Phm³, Anne Sonderskov B. Sc. ⁴

¹Director, Pharmacy Services, Rouge Valley Health System

ABSTRACT

This study was conducted at Centenary Health Centre of the Rouge Valley Health System, a community based hospital in Toronto. In January 1997, a new treatment was introduced for the management of patients with uncomplicated deep vein thrombosis (DVT). Eligible patients presenting at the ER were placed on LMWH (tinzaparin) and followed at home. Previously the patients had been hospitalized and treated with intravenous heparin until they reached a therapeutic international normalized ratio (INR). The intent of this study was to evaluate the patient outcomes and cost-savings of the new approach.

Methods

Data from all patients eligible for home care, treated in 1996 were assembled and compared with those from all eligible patients treated from April 1, 1997 to March 31, 1998. The data was collected by chart review and consisted of patient outcomes and costs during the period of heparin treatment. Costs for hospitalized patients were based on a per diem. For home care patients, the costs were itemized according to service and medication usage. All costs were calculated in 1999 Canadian dollars.

Results

In each one year period, 39 cases were treated. There was no serious adversity and the outcomes were compatible with what has been reported in the literature. The mean cost per patient for the 1996 hospitalized cohort was \$3,266 compared to \$584 for the subsequent home care cohort. The difference was statistically significant (p<0.00001).

Conclusion

Home care with tinzaparin compared to hospital care with IV heparin resulted in a large mean saving per patient with no difference in outcome.

Key Words: Deep Vein Thrombosis (DVT), Low Molecular Weight Heparin (LMWH), Tinzaparin Home care, Cost savings

It has been reported that the subcutaneous administration of low molecular weight heparin (LMWH) products in a standard dosage in the treatment of deep vein thrombosis (DVT) can reduce or eliminate the need for hospitalization as well as significantly reduce health care costs. Studies comparing home administration of LMWH to in-hospital intravenous heparin therapy have reported that both regimens are equally safe and effective

(Table 1).^{1,2,3,4}

There are also potential benefits for the patient and the treatment centre when LMWH is used in home management. Patients who receive home treatment are more comfortable and experience higher levels of physical and social activity.² Additionally, both the patient and the health care institution may accrue certain financial advantages (Table 2).

This study reports on the experience with a home care program using LMWH (tinzaparin) at

²Clinical Co-ordinator, Centenary Health Centre Site

³Formulary Management Pharmacist, Centenary Health Centre Site

⁴Senior Pharmacy Technician, Centenary Health Centre Site

the Centenary Health Centre Site (CHC) of the Rouge Valley Health System in the treatment of uncomplicated DVT. CHC is a 400 bed community based general hospital in eastern Toronto serving a population of approximately 200,000 people. It is also a referral centre for smaller outlying hospitals.

The study was undertaken to provide an estimate of cost savings to the Health Care System as well as to examine the outcomes in treatment of DVT from using LMWH (tinzaparin) administered at home according to the standardized patient management procedures used at CHC. In 1992, CHC instituted a formal program to train and certify pharmacists in the administration and dosing of warfarin, according to a standardized nomogram, to attain a therapeutic international normalized ratio (INR). Based on this training, the attending physician could dose the patient's warfarin or could delegate the dosing to a certified pharmacist. For home care, the dosage adjustment of warfarin has been done routinely by the assigned pharmacist. However, whether the patient is treated in hospital or at home, the patient's physician always retains control over and responsibility for the patient's care.

Prior to January 1997, patients diagnosed with DVT were treated at CHC according to then standard procedures. They were admitted to the hospital and treated with dose adjusted intravenous heparin given continuously with concomitant warfarin therapy^{5,6,7} until a therapeutic INR range (>2.5-3.5) was achieved. The length of stay (LOS) in hospital was usually about 5-7 days.

Beginning in January 1997, a new treatment protocol using LMWH (tinzaparin) and home care was instituted for the treatment of uncomplicated DVT. The patient eligibility criteria for home care are based on those published by Levine et al. ¹ and are listed in the study inclusion and exclusion criteria described

in the Methods section. After being clinically diagnosed with suspect DVT in the emergency unit (ER), the patient receives one dose of tinzaparin and is scheduled for a Doppler test to confirm the diagnosis. If the test is not immediately available, the patient may be kept overnight in the ER or on an inpatient unit. Alternatively, the patient may elect to go home and return the next day for the Doppler test. With a positive diagnosis, the patient is sent home on tinzaparin with a supply of 50 tablets of warfarin, 2mg.

At home the patient is visited daily by a nurse who assesses the patient and administers the tinzaparin and a phlebotomist who takes a blood sample for INR measurement. The INR result is faxed to the hospital pharmacy, where a hospital pharmacist calls and instructs the patient on the warfarin dose for that day. Once the patient's INR is in the therapeutic range, the pharmacist contacts the patient's family physician to arrange for a smooth transition of care.

METHODS

This study was designed to describe and compare the new home-based management system at CHC with the previous hospitalization treatment for patient health care costs and outcomes. The CHC Ethics and Research Committees reviewed and approved the study protocol. The design is a historical cohort study based on chart review. As a pharmacoeconomic study, the perspective is that of the provincial government with the exception of outpatient drug expenses as described in the discussion. The study is a cost minimization study and deals with direct health care costs. The study groups are: (1) the pregroup consisting of all patients eligible for home care treated in the one year period from January 1 to December 31, 1996 before home care was available; and (2) the post-group, all similarly eligible patients treated between April 1, 1997 and March 31, 1998.

TABLE 1: Trials Studying the Use of LMWH in the Home Treatment of Deep Vein Thrombosis

veni rinemiscole					
	Levine, et al., 1996		Koopman, et al., 1996		
	enoxaparin*	IV heparin	nadroparin*	IV heparin	
n =	247	253	202	198	
recurrent thromboembolism	5.3%	6.7%	6.9%	8.6%	
major bleeding	2.0%	1.2%	0.5%	2.0%	
mean LOS (days)	1.1	6.5	67% reduction in L	MWH group	

^{*}enoxaparin and nadroparin are LMWH products

TABLE 2: Potential Savings and Costs when Treating DVT at Home with LMWH

Perspective	Cost / Savings
Hospital	Costs X LMWH more expensive than heparin Savings X Reduction in LOS X Reduction in lab tests (IV heparin requires careful monitoring of aPPT & CBC) X Reduction in IV administration costs (equipment and heparin bags)
Patient	Costs X May have to pay for LMWH Savings X Reduction in time away from work

To avoid the revised treatment transition period, the study does not include patients diagnosed between January 1, 1997 and March 31, 1997.

Study Group Assembly and Data Collection

Listings of all subjects who presented with DVT in the ER during the specified periods were assembled based on the ICD 9 Code 453.8. All subjects had a positive clinical diagnosis and a Doppler. Patients who developed DVT while in hospital were excluded. Subjects who satisfied the criteria for home treatment (Table 3)¹ according to their medical records were entered into the study. The patient chart reviews and the eligibility decisions and data collection were performed by participating hospital pharmacists (SM and AK). Both staff pharmacists were experienced in anticoagulation therapy and were certified to manage anticoagulant dosing for CHC patients.

Subjects were included in either the pre-group

or the post-group according to the date of presentation. Subjects could be included more than once in either or both groups provided that the attending physician diagnosed the presenting DVT as a new clinical event occurring during the study period (see results). The patient's charts were reviewed and data, either as described or as assigned an ICD code, were recorded on a predesigned form. The data collected were:

- Age, sex, number of co-medications and comorbidities
- Number of pertinent lab tests
- Daily and total dosage of medications for the management of DVT
- Length of stay (LOS) in hospital
- Number of days of home therapy
- Number of nurse and phlebotomist home visits
- Adverse events
- Costs

To assure patient confidentiality, since there was study input by external consultants, study forms were identified only by code number.

Patient Follow-up and Outcomes

Patients in the home care group were followed until they attained a therapeutic INR value. Patients in hospital were followed until their INR was in the therapeutic range or until the treating physician discharged the patient if that occurred early (see results).

Any related adverse health events reported in either the hospital chart or the pharmacist/nurse's home follow-ups during this period were recorded. Events to be recorded included: death, related rehospitalization, thromboembolic episodes, pulmonary embolism and bleeding. Because of restricted follow-up any adverse events reported beyond this period were not systematically collected. For the small number of patients discharged from hospital early without hospital follow-up, adverse events are not possible to determine.

Cost Assessment

Costs reported are in 1999 Canadian dollars.

Hospital costs are based on a mean cost per bed including all nursing care, meals, lab tests, medications, etc. Because of the hospital methods for recording costs it is not possible to itemize specific costs for each hospitalized patient. The cost per patient hospital day is \$660, based on CHC's 1998 - 1999 fiscal financial report to the Ontario Ministry of Health. The cost per bed is the same in the intensive care unit, ER, or on the ward. The daily census for occupied beds is determined at midnight. The costs for home care patients were calculated on an itemized basis for each patient's resource usage, i.e. hospital bed usage for patients who occupied a bed at the time of the bed census, home nurse visits, phlebotomist visits, and amount of drug used. The cost of the nurse visit (\$40) and the phlebotomist home visit (\$29), which includes the cost of the INR test, were obtained from the hospital's regional Home Care Contractor.

The cost of drugs, warfarin (Coumadin[®]) and LMWH (tinzaparin), is based on the Ontario Drug Benefit Formulary with a \$6.47 dispensing fee. At the time of the study there was no 10% markup over the pharmacy cost for limited use medication. Since there was no difference in time commitment between hospitalized patients and home care patients, the cost for the pharmacists' time was not included. Costs for physician billing in the hospital were not known and are not included.

RESULTS

Study Population

A total of 129 charts with a presenting diagnosis of DVT was identified for the two study periods with 65 in the pre-group (January to December 1996) and 64 in the post-group (April 1997 to March 1998). Of the 65 cases in the pre-group, 39 cases consisting of 39 different patients satisfied the eligibility criteria for home care and hence the inclusion and exclusion criteria for study participation (Table 3). Of the 64 post-group there were 39 different eligible patients. One patient was included in both the pre-and post-groups.

All 39 cases in the pre-group were hospitalized and treated with IV heparin. Of the 39 post-group

cases, 32 were treated with tinzaparin at home and 7 were treated with either tinzaparin or IV heparin in hospital (Table 4). These seven cases satisfied the inclusion criteria according to the chart reviews. Their reasons for hospitalization are undocumented.

Table 5 presents the comparative characteristics of the treated patients. Apart from the sex distribution, the groups appear to differ only in the lower proportion of patients with co-morbid conditions in the tinzaparin home care post-group as compared with both the pre and post hospitalized groups. This difference could be due to more complete history taking and recording of data on the hospital wards than in the ER. This interpretation is speculative but is supported by the comparable proportion of co-medication usage recorded between home care subjects and hospitalized subjects in both the pre- and post-groups.

Patient Outcomes Effectiveness

The length of follow-up for each of the treated groups is presented in Table 6. The days of followup were calculated from the first day of contact to the last day of contact. There was no difference between groups in the time to reaching a therapeutic INR. The range of follow-up was quite narrow in the post group patients, 4 to 8 days; however, the time of management and follow-up was broader in the pre-group. Four patients were discharged from hospital after a short period. Three patients were discharged after one day and a further one after two days. These patients were all younger and without complicating illness. One patient remained in hospital for sixteen days due to complications of the DVT. Another patient staved ten days because of difficulty in reaching a therapeutic INR.

Untoward Events

This study focused on the acute treatment phase of DVT with no opportunity, due to confidentiality, to systematically collect information about later outcomes. However, if there was pertinent information in the patient records about a subsequent contact, this was recorded. During the

acute observation period, there were no deaths or major bleeding episodes in either group. In the pregroup one hospitalization was extended because of leg swelling and discomfort after the discontinuation of heparin. One patient discharged after one day was readmitted two days after discharge with a probable pulmonary embolism.

In the home care post-group, there were two hospitalizations occurring the next day after transfer of care to the family doctor. One case was due to spread of the DVT to the femoral area, and the other was due to a subtherapeutic INR. There were two patients with reported skin bruising during the study period. According to a review of the charts, one post-group patient was hospitalized with leg swelling 17 days after transfer of care to the family doctor. There were no untoward events reported for the post-group treated in hospital.

TABLE 3: Inclusion/Exclusion Criteria

I. Inclusion Criteria

Diagnosed with DVT in the ER in the appropriate time frames

i) Pre-Group - January 1 to December 31, 1996 Post-Group - April 1, 1997 to March 31, 1998

II. Exclusion Criteria¹

- 1. Co-morbid illness requiring hospitalization
- Suspected pulmonary emboli (other thromboembolic episode)
- 3. Hemodynamically unstable (MI, thrombotic stroke)
- 4. Active bleeding (GI haemorrhage, intracranial haemorrhage)
- 5. Active peptic ulcer
- 6. Age < 18
- 7. Pregnancy
- Suspicion of poor patient understanding or compliance

Geographical inaccessibility to home care / lab testing.

TABLE 4: Study Subjects

	Pre-new protocol group	Post-new protocol group	
Study Groups	IV Heparin	LMWH	
Dates for inclusion	January 1996 to December 1996	April 1997 to March 1998	
Charts reviewed	65	64	
# Eligible case	39	39	
# Patients	39	39	
Treatment Site	Hospital 39	Home 32 /Hospital 7	

Table 5: Patient Characteristics

		Pre-LMWH	Post-LMWH Protocol	
Study Gr	Study Groups		Home	Hospital
Patients		39	32	7
Events		39	32	7
	Range	20 - 92	31 - 81	25 - 79
	Mean	59.36	60.72	54.71
Age	Median	60	66	61
	Male	13	18	3
Sex Female		26	14	4
% patients with one or more co-medications		72%	72%	71%
% patients with one or more co-morbid states		79%	53%	71%

TABLE 6: Days Followed for Care

Study Groups	Pre-LMWH Protocol	Post-LMWH Protocol		
Rx Site	Hospital	Home (a)	Hospital (b)	Both (a+b)
Follow Days	233	191	38	229
Range per patient	2-17	4-8	4-7	4-8
Mean per patient	5.97	5.96	5.43	5.87
Median per patient	6	6	5	6

TABLE 7: Hospital Days For Costing

		Post-LMWH Protocol		
Study Groups	Pre-LMWH Protocol	Home (a)	Hospital (b)	Both (a+b)
Number of Cases	39	32	7	39
Days in Hospital	193	8	31	39

TABLE 8: Cost Comparison

TABLE 6. GOST GOTTPATISON	Pre-Group (Jan to Dec 1996)	Post-Group (Apr 1997 to Mar 1998))
	(6411 to 200 1000)	(, 15.	1007 to Mai 1000	,
Study Groups	Hospital	Home (a)	Hospital (b)	Both (a+b)
Hospital Care @ \$660/day	\$127,380	\$5,280	\$20,460	\$25,740
Nurse Visits @ \$40/visit		\$5,120		\$5,120
Phlebotomy Visits @ \$29/visit		\$4,147		\$4,147
Warfarin (Coumadin [®]) @ 50 (2mg tabs) x \$0.3292+\$6.47		\$734		\$734
LMWH (tinzaparin) @ \$32.00/vial + \$6.47		\$3,407		\$3,407
Total	\$127,380	\$18,688	\$20,460	\$39,148
Mean per patient	\$3,266	\$584	\$2,923	\$1,004
Median per patient	\$3,300	\$429	\$2,640	\$459
Standard Deviation	\$1,752	\$338	\$644	\$993
Range per patient	\$660-\$10,560	\$300-\$1,681	\$1,980-\$3,960	\$300- \$3,960

TABLE 9: Cost Sensitivity Analysis

One and Two Way Sensitivity Analysis of the Difference in Average Cost per Patient between Post and Pre Combined Groups				
Post Combined Costs	Pre Group Costs	Average Cost per Patient		
Low	Low	-\$1,503		
Low	Mean	-\$3,255		
Low	High	-\$5,008		
Mean	Low	-\$510		
Mean	Mean	-\$2,262		
Mean	High	-\$4,015		
High	Low	\$483		
High	Mean	-\$1,270		
High	High	-\$3,022		

TABLE 10: Summary Count of Lab Tests in Hospital Treatment vs. Home Care

Study Groups	Pre-LMWH Protocol	Post-LMWH Protocol	
Rx Site	Hospital	Home	Hospital
Cases	39	32	7
Lab Tests	583	213	107
Tests / Case	14.9	6.7	15.3

TABLE 11: Difference in Type and Numbers of Lab Tests between Hospital and Home Care

Study Groups	Pre-LMWH Protocol	Post-LMWH Protocol	
Rx Site	Hospital	Home	Hospital
аРТТ	260	16	49
CBC	106	26	13
INR	206	171	39
CT Abd & Pelvis	-	-	1
CT Head	-	-	1
US Abd / Pelvis	6	-	2
Chest X Rays	3	-	1
Lung scan	-	-	1
Pulmonary Function Test	1	-	-
Doppler	1	-	-

Costs

Of the 32 home care patients in the post-group, 30 were discharged from the ER on day one and 2 were kept at the hospital. Of these, one patient spent less than 24 hours awaiting a Doppler test; the second had a history of DVT while on warfarin and was kept for observation for less than 48 hours. Five of the patients discharged on day one occupied a bed at midnight and were counted as hospitalizations according to the hospital census method. Days of hospitalization according to the hospital census count are presented in Table 7.

A summary of patient treatment costs is presented in Table 8. The total cost for the 39 cases treated before the introduction of home care was \$127,380. After the implementation of the new protocol, the total cost for the same number of cases, including both home care and hospitalization, was \$39,148. Using the Wilcoxon Rank Sum test, comparison of the

mean cost per patient (\$3,266) in the pre-period with the mean cost per patient in the post period, both for home care (\$584) and for home care and hospital combined (\$1,004) were statistically significant with a p value <0.00001. There was no statistical difference in the per patient cost for hospitalized patients in the pre and post period.

Table 9 presents a sensitivity analysis comparing the pre group with the combined post group both hospitalized and cared for at home. High, mean and low values for the post combined cost equal the mean + SD, the mean, and the mean - SD respectively, where the SD is the variables standard deviation. The pre-group cost variable is defined in the same manner.

In assessing hospital costs versus home care costs, the question was raised whether hospital costs are incrementally higher because, during their management, hospitalized patients are likely to have more lab tests than home care patients. The number of tests related to patient

management (excluding the initial Doppler) is presented in Tables 10 and 11. The tables include initial tests done in the hospital for home care patients. Table 10 presents a summary count of tests. Table 11 lists those tests.

DISCUSSION

This study is based on historical recorded data and is subject to the limitations of such studies. However, the data were collected from the original patient records by reviewers who were knowledgeable in the field and had hands on experience. The two cohorts that were compared were not treated concurrently but there is no evidence to suggest that there were any systematic changes over time that would effect the endpoints other than the intervention being studied.

On comparison, the two groups, before and after the introduction of the home care protocol, do not differ in ways that would effect outcomes of interest. Further, the costs for patients treated in hospital for the pre and post groups are very similar.

The small sample size of this study and, therefore, the limited power, makes conclusive comparisons of adverse outcomes between home care and hospital care inappropriate. It is estimated that, to show doubling of differences in important adversity would require hundreds to thousands of patients per group depending upon the outcome of interest e.g. major bleeds. Nevertheless no differences in health outcomes (i.e., attainment of a therapeutic INR and occurrence of untoward events) between the groups were observed and these findings are compatible with the published literature.^{1,2}

Using a careful and as itemized a measurement of costs as possible, the home care treatment costs are seen to be significantly lower than hospital treatment. For the treatment of 39 cases for one year in each of the pre and post periods, the cost difference was \$88,232

(\$127,380 - \$39,148) p<0.00001 including the costs for seven patients in the post period who were considered on review to be eligible for home care but were treated in hospital (Table 8).

This amount was all cost savings to the health care system except for the costs of the outpatient drugs, warfarin and tinzaparin. These were cost shifts and amounted to \$4,141. The mean cost per patient in the post period year was \$1,004 including the seven eligible patients who were hospitalized, compared to \$3,266 in the pre period year. This difference is statistically significant with a p value of <0.00001 and is confirmed in the sensitivity analysis (see Table 9).

Since the number of eligible patients who might be hospitalized in any given time period is not a predictable constant the total savings and per patient costs are not predictable. However, more striking and not subject to this variability, is the difference in mean patient cost between home treatment with LMWH (tinzaparin) and hospital treatmentwith IV heparin: \$2,682 (\$3,266 versus \$584) p,0.00001. The hospital cost is about 5 and a half times the home cost. The difference in lab tests between hospitalized and tinzaparin home care patients raises a question that a possible contributor to hospital costs is an increased likelihood of laboratory tests for hospitalized patients. The mean number of lab tests per home care patient was 6.7. For hospitalized patients in the pre- and post-groups, the mean number of lab tests was, respectively, 14.9 and 15.3.

CONCLUSION

Treating appropriate patients for DVT on an outpatient basis using a combination of LMWH (tinzaparin) and warfarin (Coumadin®) results in large cost savings for the health care system with no apparent change in effectiveness or adversity.

ACKNOWLEDGEMENTS

The investigators thank Dr. E. Keith Borden, Toronto consultant, for his advice and assistance in the design, conduct and manuscript preparation of this study and Dr. J. G. Heller for his statistical and cost sensitivity analyses. The authors thank Dr. Peter Anglin and Dr. Eric Goode for their support and assistance in the design of the Outpatient DVT Management Program. The authors thank the Warfarin Team members for their support and ongoing excellent work. This study was funded in part by Leo Pharma Inc.

REFERENCES

- Levine M, Gent M, Hirsh J, et al. A comparison of low molecular weigh heparin administered primarily at home with unfractionated heparin administered in the hospital for proximal deep vein thrombosis. N Engl J Med 1996; 334: 677-81.
- A. Koopman MM, Prandoni P, Piovell F, et al. Treatment of venous thrombosis with intravenous unfractionated heparin administered in the hospital as compared with subcutaneous low

- molecular weight heparin administered at home. N Engl J Med 1996; 334; 682-7.
- 3. Rose P, Bell D, Green ES, et al. The outcome of ambulatory DVT management using a multidisciplinary approach. Clinical & Laboratory Haematology 2001; 23:301-6.
- 4. Tillman DJ, Charland SL, and Witt DM. Effectiveness and economic impact associated with a program for outpatient management of acute deep vein thrombosis in a group model health maintenance organization. Arch Int Med 2000; 160: 2926-32.
- 5. Hyers TM, Hull RD, Weg JG. Antithrombotic therapy for venous thromboembolic disease. Chest 1995; 4 (Suppl): 335s-51s.
- 6. Hull RD, Pineo GF. Low molecular weight heparin for the treatment of venous thromboembolism. Sem Resp Critical Care Med 1996; 17070.
- 7. Hyers TM, Agnelli G, Hull RD, et al. Antithrombotic therapy for venous thromboembolic disease. Chest 1998; 114: 561s-78s