CONTEMPORARY SUBJECT

Effect of a Clinical Pharmacy Education Program on Improvement in the Quantity and Quality of Venous Thromboembolism Prophylaxis for Medically Ill Patients

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ABSTRACT

OBJECTIVE: The American College of Chest Physicians (ACCP) recommends unfractionated heparin (UFH) or low-molecular-weight heparin (LMWH) for prevention of venous thromboembolism (VTE) in medically ill patients. Despite these recommendations, a previous analysis at our institution revealed a low utilization of VTE prophylaxis in medically ill patients. Our objective was to evaluate the effects of a pharmacy-driven education program on the quantity and quality of VTE prophylaxis in medically ill patients.

METHODS: An educational program focusing on the importance of VTE prophylaxis in medically ill patients was developed by clinical pharmacists and presented to nurses, pharmacists, and physicians in a 493-bed community teaching hospital. The educational program was conducted between June 2002 and June 2003 and consisted of in-service presentations, newsletters, and quality assurance presentations on VTE prophylaxis. The educational program focused on 4 main points: (1) hospitalized medically ill patients are at risk for developing VTE, (2) how to identify medically ill patients who require VTE prophylaxis, (3) the fact that VTE prophylaxis is currently underutilized in medically ill patients, and (4) appropriate VTE prophylaxis strategies for medically ill patients. A posteducation retrospective chart review was performed in medically ill patients with discharge dates between October 2003 and March 2004, and these posteducation medical chart data were compared with the results from a preeducation analysis of patents with discharge dates from January 2001 to March 2002. Data collection included patient demographics, VTE risk factors, and use and type of VTE prophylaxis.

RESULTS: The posteducation retrospective chart review was performed for 297 medically ill patients with discharge dates between October 2003 and March 2004 and for 344 preeducation patients discharged between January 2001 and March 2002. Patient demographics and primary diagnoses were similar between the preeducation and posteducatin groups. The mean number of risk factors per patient in the preeducation group was 2.53 ± 0.96 versus 2.38 ± 0.88 in the posteducation group ($P=0.626$). Pharmacy education was associated with an increase in the utilization of any VTE prophylaxis (43% in the preperiod vs. 58% in the postperiod; $P<0.001$). Prophylaxis judged to be suitable (UFH 5,000 units twice daily, or UFH 5,000 units 3 times daily, or LMWH once daily), increased from 38% in the preeducation period to 49% in the posteducation period, $P=0.006$). Prophylaxis judged to be optimal (UFH 3 times daily or LMWH once daily) increased from 11% to 44% of patients, $P<0.001$).

CONCLUSIONS: A hospital-wide clinical pharmacy education program was associated with significant improvement in the quantity and quality of VTE prophylaxis in medically ill patients in a community teaching hospital.

KEYWORDS: Venous thromboembolism, Venous thromboembolism prophylaxis, Medically ill, Pharmacy education, Pharmacy intervention

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Venous thromboembolism (VTE), encompassing both deep vein thrombosis (DVT) and pulmonary embolism (PE), affects approximately 2 million Americans annually.[1,2] Data indicate that only 280,000 to 300,000 of the 2 million patients (14% to 15%) who experience VTE are objectively diagnosed with VTE.[2] VTE is often a silent, yet potentially fatal disease. When symptoms do occur, they are often nonspecific and the first manifestation of the disease may be death.[3] Due to the significant morbidity and mortality associated with VTE, prevention is critical.

Several groups of patients, such as those undergoing orthopedic surgery, general surgery, and experiencing acute myocardial infarction, are known to be at high risk for VTE.[1] General medical patients, or the medically ill, are a much more heterogeneous group of patients whose VTE risk is often not assessed. Despite inadequate assessment in the clinical environment, medically ill patients have a moderate-to-high risk of developing VTE.[1] In trials in which a placebo or no therapy was given, the incidence of VTE during hospitalization has been 10% to 26%.[4-6]

While some of these trials are decades old, the more recent MEDENOX (Prophylaxis in Medical Patients with Enoxaparin) Trial confirmed that, in current practice, medically ill patients are still at risk for VTE.[6] Medically ill patients in MEDENOX were generally admitted with severe congestive heart failure (34%), acute respiratory failure that did not require ventilator support (53.5%), or acute infection without septic shock (53%). The 1,102 patients in this trial were randomized to either placebo or 1 of 2 doses of enoxaparin for VTE prophylaxis. The placebo group in MEDENOX revealed an in-hospital total VTE rate of 14.9% and a proximal DVT rate of 4.9%. Therefore, a thromboembolic event was documented in 1 of every 6 medically ill patients randomized to placebo.

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TABLE 1 Sample Selection

	Total Number of Patients (% of Total): Preeducation	Total Number of Patients (% of Total): Posteducation
Inclusion criteria		
Primary diagnosis of HF	159 (36.4)	163 (43.2)
Primary diagnosis of ARF	76 (17.4)	68 (18.1)
Primary diagnosis of pneumonia	202 (46.2)	146 (38.7)
Total before exclusion criteria	437 (100.0)	377 (100.0)
Exclusion criteria		
Admitted with anticoagulation for AF	79 (18.1)	70 (18.6)
Admitted with anticoagulation for stroke	8 (1.8)	6 (1.6)
Admitted with anticoagulation for MHV	6 (1.4)	4 (1.1)
Total patients selected	344 (78.7)	297 (78.8)

AF = atrial fibrillation; ARF = acute respiratory failure; HF = heart failure; MHV = mechanical heart valve.

TABLE 2 Patient Characteristics

Characteristic	Preeducation (January 2001-March 2002) (n = 44)	Posteducation* (October 2003-March 2004) (n = 297)
Age (years)	77 ± 12	77 ± 13
Gender (% male)	36	38
Weight (kg)†	76.4 ± 26	74.1 ± 25
Height (inches)†	66 ± 4.6	66 ± 4.4
Mean LOS (days)†	9.7 ± 4.7	9.5 ± 5.5
Primary diagnosis (%)		
Acute respiratory failure	18	20
Heart failure	26	32
Pneumonia	56	48
VTE risk factors (%)		
Immobility	34	29
Previous VTE	4	7
Cancer	7	10
Obesity	25	20
Heart failure	69	68
Central venous catheter	6	2
Estrogen use	7	2
Other‡	4	4

** P >0.1 for all comparisons.*
† Mean LOS, weight, and height were compared using the Mann-Whitney U test. All other variables were compared using the chi-square test.
‡ "Other" represents the category of major surgery, irritable bowel syndrome, nephritic syndrome, documented thrombophilia, and documented varicose veins as risk factors.
LOS = length of stay, VTE = venous thromboembolism.

The American College of Chest Physicians (ACCP) currently recommends that every hospital develop specific strategies for assessing VTE risk and also plan for implementation of appropriate prophylaxis.[1] ACCP currently recommends unfractionated heparin (UFH) or low-molecular-weight heparin (LMWH) for prevention of VTE in medically ill patients.[1] Despite these ACCP recommendations, the administration of prophylaxis in medically ill patients remains underutilized.[7,8]

A previous analysis at our 493-bed community teaching hospital revealed a low utilization of VTE prophylaxis in medically ill patients.[9] In the previous analysis, only 43% of medically ill patients received any type of VTE prophylaxis, and only 11% received optimal prophylaxis. The clinical pharmacy department developed a hospital-wide education program to address the underutilization of VTE prophylaxis in these patients. We hypothesized that this educational strategy would increase both the quantity and quality of VTE prophylaxis.

Methods

Data on patients in the preeducation group were collected by a retrospective chart review for patients with discharge dates between January 2001 and March 2002 in this 493-bed community teaching hospital. Patients were included in this analysis if they met the MEDENOX criteria for defining medically ill: (a) had to be at least 40 years old, (b) had a hospital stay of at least 6 days in other than an intensive care unit (ICU), and (c) had a primary diagnosis of acute respiratory failure (*International Classification of Diseases, Ninth Revision, Clinical Modification* [ICD-9-CM] codes 491.20, 491.21, and 518.81), heart failure (ICD-9-CM codes: all of 428), or bacterial pneumonia (ICD-9 code 482.9). Patients were excluded if there was a clear indication for receiving anti-coagulation, i.e., patients with a history of atrial fibrillation, mechanical heart valve, or stroke, or who were on warfarin at home and continued during the hospitalization. Patients with contraindications to anti-coagulation (e.g., active bleeding or thrombocytopenia) were also excluded (Table 1). Data were also collected on patient demographics, presence of ACCP-recognized VTE risk factors (i.e., immobility, history of VTE, presence of cancer, obesity, heart failure, current central venous catheter, estrogen use, major surgery, irritable bowel syndrome, nephritic syndrome, documented thrombophilia, and documented varicose veins), and length of stay (Table 2).

After identifying patients meeting the MEDENOX criteria, patient records were reviewed for the use and type of VTE prophylaxis (Table 3). "Any" VTE prophylaxis was defined as any pharmacological prophylaxis, regardless of dose, as well as any type of mechanical prophylaxis implemented for VTE prevention. "Suitable" prophylaxis was defined as either subcutaneous (SC) UFH 5,000 units twice daily, SC UFH 5,000 units 3 times daily, or SC enoxaparin. We defined "Optimal" prophylaxis as either SC UFH 5,000 units 3 times daily or SC enoxaparin 40 mg once daily. These categorical definitions of type (quality) of drug prophylaxis of VTE were based on recommendations from the 6th ACCP Consensus Conference on Antithrombotic Therapy and the published medical literature.[14]

There was 1 patient in the preeducation period who received enoxaparin 30 mg twice daily and 2 patients in the

posteducation period who received the same dose. There was also 1 patient in the posteducation period who received enoxaparin 60 mg once daily. Since these 4 patients were receiving a prophylaxis dose of enoxaparin, they were included in the overall category of enoxaparin therapy. Other LMWHs were not evaluated because enoxaparin was the only LMWH on the drug formulary at the time of this analysis.

Based on the disappointing results found in the initial data collection (preeducation) period (Table 4), a pharmacy-driven education program was initiated with the intent of improving both the quantity and quality of VTE prophylaxis in medically ill patients. Patients in this initial data collection period served as the historical control (comparison) group. The education program was initiated in June 2002 and was aggressively continued until June 2003. This program utilized several different methods of education and targeted multiple health care disciplines. Live (one-to-group) educational presentations were made to nursing staff, house staff, pharmacists, and physicians. All nurses were required to attend one of these presentations. Therefore, 4 presentations were given for each of the 6 nursing divisions in the hospital. Due to the rotating nature of the house staff, 4 presentations were given to get the attendance of all 32 house staff. Four presentations were given in the pharmacy department and an additional 6 presentations at different physician meetings. These presentations focused on 4 main points: (1) hospitalized medically ill patients are at risk for developing VTE, (2) how to identify medically ill patients who require VTE prophylaxis, (3) the fact that VTE prophylaxis is currently underutilized in medically ill patients, and (4) appropriate VTE prophylaxis strategies for medically ill patients. Appropriate VTE prophylaxis strategies followed the definition for optimal prophylaxis given above (SC UFH 5,000 units 3 times daily or SC enoxaparin 40 mg once daily). During the educational presentations, no preference was given to either prophylaxis regimen.

Another form of education included newsletters, which were mailed to all 260 physicians with practice privileges at this community teaching hospital. There were also 4 presentations with roundtable discussions at quality assurance meetings for the medical staff and administration. Finally, at the time this project was conducted, clinical pharmacists participated on rounds on 2 of the 4 cardiology services and 3 of the 5 internal medicine services. In the course of providing pharmaceutical care to patients on these inpatient services, recommendations on the need for prophylaxis and type of prophylaxis for individual patients were often given by the clinical pharmacists.

Clinical pharmacists and house staff often rotated to different teams at the beginning of each month. This provided the opportunity to interact with more house staff and attending physicians than if they had stayed on one team consistently. The primary outcomes desired by this pharmacy-driven education program were an increase in the quantity and quality of VTE prophylaxis provided to medically ill patients, as defined in the published literature.

TABLE 3 Study Definitions

Any prophylaxis	All pharmacological or mechanical strategies
Suitable prophylaxis	Unfractionated heparin 5,000 units twice daily, or unfractionated heparin 5,000 units 3 times daily, or enoxaparin 40 mg once daily
Optimal prophylaxis	Unfractionated heparin 5,000 units 3 times daily; or enoxaparin 40 mg once daily

"Suitable prophylaxis" is defined on the basis of the American College of Chest Physicians (ACCP) 6th Consensus Conference recommendations for providing venous thromboembolism prophylaxis in medically ill patients.[14] "Optimal prophylaxis" is defined on the basis of the medical literature, including the summary data in Table 6.

TABLE 4 Improvement in the Quantity and Quality of VTE Prophylaxis: Percentage of Patients Receiving VTE Prophylaxis

Type of Prophylaxis	Preeducation (n = 344)	Posteducation (n = 297)	*P* Value*
Any prophylaxis	43% (148)	58% (172)	<0.001
Suitable prophylaxis†	38% (131)	49% (146)	0.006
Optimal prophylaxis†	11% (38)	44% (131)	<0.001

** The chi-square test was used to make comparisons between the 2 groups.*
† Defined in Table 3.
VTE = venous thromboembolism.

TABLE 5 Breakdown of Patients Receiving "Suitable" Prophylaxis: Percentage Improvement in the Quality of VTE Prophylaxis

Type of Prophylaxis	Preeducation (n = 131)	Posteducation (n = 146)	*P* Value*
UFH twice daily	74% (97)	10% (15)	<0.001
UFH 3 times daily	18% (24)	20% (29)	0.863
Enoxaparin once daily	8% (10)	70% (102)	<0.001

** The chi-square test was used to make comparisons between the 2 groups.*
UFH = unfractionated heparin; VTE = venous thromboembolism.

A follow-up evaluation of the utilization of VTE prophylaxis in medically ill patients was then conducted. Another retrospective review was conducted on patients with discharge dates between October 2003 and March 2004 (posteducation group). Patients were identified using the same criteria as in the preeducation period (MEDENOX criteria). As in the initial evaluation, data were collected on patient demographics, presence of VTE risk factors, length of stay, use of VTE prophylaxis, and type of VTE prophylaxis utilized. Results from findings in the posteducation group were then compared with findings in the preeducation group (historical comparison group). All data collections were approved by the institution's investigational review board.

Comparisons between the 2 groups on the use of VTE prophylaxis, type of VTE prophylaxis, primary diagnosis, presence of VTE risk factors, and dichotomous patient characteristics (age and gender) were accomplished using the chi-square test. Mean length of stay, patient weight, and patient height were compared using the Mann-Whitney *U* test. An a priori *P* value of <0.05 was considered statistically significant.

Results

There were 437 patients identified in the preeducation period and 377 patients in the posteducation period. Of these, 93 patients (21.3%) in the preeducation period and 80 patients (21.2%) in the posteducation period were excluded from analysis due to a clear indication for already receiving warfarin therapy on admission (Table 1). No patients in either group had a contraindication to VTE prophylaxis.

Data were available for 344 patients in the preeducation period (historical comparison group) and 297 patients in the posteducation period. Patient demographics were not significantly different between the groups for all comparisons (Table 2). Overall, patients were, on average, 77 years old, weighed 75 kg, and had a length of stay of 9 to 10 days. About two thirds of the patients were female. While there were numerically more patients with the primary diagnosis of pneumonia in the preeducation group and more patients with heart failure in the posteducation group, these differences were not statistically significant. Patients in the preeducation group had, on average, 2.53 ± 0.96 VTE risk factors. Patients in the posteducation group had a similar number of mean VTE risk factors, 2.38 ± 0.88 ($P = 0.626$). While there were also small numerical differences between the groups with regard to existing risk factors for VTE, no statistically significant differences existed between the groups (Table 2).

The quantity of VTE prophylaxis was significantly improved in the posteducation period compared with the preeducation period, regardless of how VTE prophylaxis was defined (Table 4). The pharmacy-driven education program was associated with a significant 26% relative increase in the utilization of any VTE prophylaxis ($P < 0.001$) and a 22% relative increase in suitable VTE prophylaxis ($P = 0.006$). The most impressive improvement in the quantity of VTE prophylaxis was the significant 75% relative increase in the utilization of optimal VTE prophylaxis ($P < 0.001$).

In addition to improving the quantity of VTE prophylaxis, we also sought to improve the quality of VTE prophylaxis with our pharmacy-driven education program. During the initial data collection, the majority (74%) of suitable VTE prophylaxis was UFH twice daily. Based on the current literature, this was not considered optimal prophylaxis. Part of our educational program emphasized the utilization of UFH 3 times daily or LMWH once daily, and not the use of UFH twice daily. As a result of this educational program, there was a significant 86% relative reduction in the utilization of UFH twice daily (Table 5). When clinicians were given the choice between UFH 3 times daily and enoxaparin once daily, the majority chose the once-daily regimen. There was only about a 10% relative increase in the use of UFH 3 times daily ($P = 0.863$), while there was more than an 8-fold increase in the use of enoxaparin once daily ($P < 0.001$). The significant reduction in the use of UFH twice daily and the significant increase in the use of optimal prophylaxis (mainly enoxaparin once daily) represents our ability to improve both the quality of prophylaxis along with the quantity of prophylaxis in these medically ill patients.

Discussion

Several retrospective reviews have reported a 30% to 45% prophylaxis utilization rate in medically ill patients.[9-11] However, few institutions have documented the success of a program that addresses the low utilization rates of prophylaxis. Furthermore, even fewer investigations have designed an educational program that targets both the quantity and quality of VTE prophylaxis. Our initial prophylaxis rates are not unusually low, as others have reported similar starting points. Coincidentally, 3 independent retrospective chart reviews have reported that only 43% of their medically ill patients received any type of VTE prophylaxis.[9-11]

Rahim and colleagues retrospectively evaluated VTE prophylaxis rates in medical in-patients admitted consecutively to the medicine units at 2 teaching hospitals. These medically ill patients were defined as patients admitted to the medical ward with a number of different diagnoses, including cerebrovascular disease, heart failure, general infection, diabetes, malignancy, or chronic obstructive pulmonary disease. During a period of time similar to our initial preeducation data collection period, they reported that the utilization of any prophylaxis improved according to the number of risk factors identified, from 25% in low-risk patients to 43% in high-risk patients. Their conclusion was that a risk-factor-based classification scheme might be helpful in increasing their institutions' poor VTE prophylaxis rates by helping physicians identify those patients at risk.

Stinnett and colleagues conducted a similar study with an objective to evaluate the impact of an awareness campaign on prophylaxis rates.[11] A combination of interventions that included an educational component, risk-stratification guidelines, and standard admission order sets, were implemented. During the preintervention phase, 43% of medically ill patients, who were defined as patients aged 18 years or older who had been admitted to cardiology, oncology, or general medical services for greater than 48 hours, received some form of prophylaxis. Similar to our initial data collection, the majority of prophylaxis consisted of UFH twice daily. An improvement was observed in the postintervention phase, revealing that 71% of the medically ill patients received some form of VTE prophylaxis. Furthermore, the utilization of preferred regimens, UFH 3 times daily and

TABLE 6 Clinical Trials Utilizing UFH Twice Daily for VTE Prophylaxis in Medically Ill Patients

Trial	Methods	Therapy*	No of Patients	End Points	Results (%) UFH	Control	*P* Value	Comments
Ibarra-Perez et al.[4] *Angiology,* 1988	Nonrandomized, unblinded	UFH 5,000 BID vs. GCS, EB vs.ASA, vs. no prophylaxis	192	VTE by RFUT	2.6	26.1	<0.05	Lack of randomization, lack of blinding, and small numbers of patient in each group present significant limitations to the influence of the trial results.
Halkin et al.[17] *Ann Intern Med,* 1982	Randomized, unblinded	UFH 5,000 BID vs. no prophylaxis	1,358	Mortality	7.8	10.9	<0.05	Randomization by medical record number and open-label design influenced patient selection into the trial, limiting the influence of the results.
Cade et al.[18] *Crit Care Med,* 1982	Randomized, double-blind, placebo-controlled	UFH 5,000 BID vs. placebo	131	VTE by RFUT	2	10	NS	Well-conducted trial did not demonstrate a benefit of UFH BID in medically ill patients.
Heparin Prophylaxis Study Group[19] *Lancet,* 1996	Randomized, double-blind	UFH 5,000 BID vs. no prophylaxis	11,693	DVT at autopsy PE at autopsy Mortality	49 7.7 5.3	49 8.5 5.3	NS NS NS	Largest VTE prevention trial ever conducted in medically ill patients. No benefit of UFH BID was evident, regardless of the end point evaluated.

** All prophylaxis doses are given subcutaneously.*
ASA = aspirin; BID = twice daily; DVT = deep vein thrombosis; EB = elastic bandage; GCS = graded compression stockings; NS = not significant; PE = pulmonary embolism; RFUT = radiolabeled ^{125}I-fibrinogen-uptake test; UFH = unfractionated heparin; VTE = venous thromboembolism.

LMWH, had increased from 10% to 47%. Interestingly, UFH 3 times daily was the preferred therapy in the postintervention phase. This study illustrates the importance and value of implementing a risk assessment component to VTE prophylaxis programs.

Education is a key component to any successful prophylaxis program regardless of clinician experience. Fassiadis and colleagues evaluated the change of VTE prophylaxis during a 6-month period after local prophylaxis guidelines were put into practice. Prophylaxis utilization remained suboptimal after the institution implemented prophylaxis guidelines without an education component.[12] Kucher and colleagues developed a computer-alert program to increase the prophylaxis of medically and surgically hospitalized patients with VTE risk factors.[13] Prophylaxis improved from 14.5% in the nonalert arm (control group) to 33.5% in the alert arm (P <0.001). This modest improvement in prophylaxis using a computer-based reminder system further underscores the value of clinician education.

As stated previously, we defined suitable VTE prophylaxis in medically ill patients as the use of UFH twice daily, UFH 3 times daily, or LMWH once daily. This definition was chosen based on the ACCP 6th Consensus Conference recommendations for providing VTE prophylaxis in medically ill patients.[14] This was the most recent version of the guidelines available at the time our project was implemented and completed. The more current ACCP 7th Consensus Conference recommendations only state that "low-dose" UFH can be used with no specific discussion of frequency as in the previous recommendations.[1] This issue has also been the topic of comprehensive reviews in the medical literature, which have questioned the role of UFH twice daily as an effective prophylaxis regimen.[15,16]

Our definition of optimal VTE prophylaxis in medically ill patients included UFH 3 times daily and LMWH once daily, but did not include UFH twice daily. Data supporting UFH twice daily is very limited (Table 6). There are only 2 clinical trials that suggest a possible benefit of UFH twice daily in medically ill patients.[4,17] One trial distributed 192 patients to control or 1 of 4 other treatment groups.[4] While there were fewer DVTs in patients receiving UFH compared with the control group, the lack of randomization, blinding, and the small number of patients per group presented significant limitations to making strong conclusions about these data. The other trial by Halkin and colleagues demonstrated a significant reduction in mortality with the use of UFH compared with no therapy.[17] While this may be considered an impressive finding, there are significant limitations to these data. Patients in this trial were randomized by medical record number which, combined with the open-label design, was demonstrated to have potentially influenced the number of patients considered eligible for treatment with UFH. Therefore, the clinical trials that suggest a possible benefit of UFH twice daily in medically ill patients have serious trial design flaws, limiting the use of this regimen in clinical practice.

There is a body of data that suggests a lack of benefit of UFH twice daily for VTE prophylaxis in medically ill patients (Table 6). Cade and associates failed to demonstrate a significant reduction in DVT in medically ill patients compared with placebo in a well-conducted randomized, double-blind, placebo-controlled trial.[18] The Heparin Prophylaxis Study Group

conducted the largest trial performed in medically ill patients.[19] In this trial, there was no reduction in DVT, PE, or mortality with the use of UFH twice daily compared with placebo. The Enoxaparin in Medicine Study Group demonstrated equal efficacy between UFH twice daily and enoxaparin 20 mg daily for VTE prophylaxis in medically ill patients.[20] These results are consistent with the findings from the MEDENOX trial in which 20 mg of enoxaparin was equal to placebo in preventing VTE in 1,102 medically ill patients.[6] Therefore, based on the available clinical evidence, a strong evidence-based recommendation cannot be made for the routine use of UFH twice daily for prevention of VTE in medically ill patients.

The efficacy of UFH twice daily as a VTE prophylactic regimen has been questioned for surgical patients as well as for medically ill patients. A meta-analysis of 49 trials with general surgery patients demonstrated a DVT frequency of 11.8% (95% CI, 10.6%-13.1%) in patients receiving UFH twice daily vs. 7.5% (95% CI, 6.4%-8.6%) in patients receiving UFH 3 times daily.[21] Data from gynecological oncology surgery trials have demonstrated a lack of benefit of UFH twice daily compared with placebo but have proven efficacy of UFH 3 times daily in this patient population.[22,23] Therefore, the efficacy of UFH in prevention of VTE appears to be dose-related.

UFH 3 times daily has demonstrated effectiveness compared with control or placebo in medically ill patients.[5,24] There are also no trials suggesting a lack of benefit with UFH 3 times daily as there are with UFH twice daily. There have been a number of trials supporting the efficacy of LMWH once daily in preventing VTE in medically ill patients.[6,25-27] Trials comparing the efficacy of LMWH once daily with UFH 3 times daily have demonstrated similar efficacy between the regimens, with a benefit of LMWH in higher-risk patients.[28-31] The evidence from these clinical trials supports our definition of optimal VTE prophylaxis in medically ill patients.

The significant increase in the utilization of optimal prophylaxis in the present study was mainly due to a more than 8-fold increase in the use of enoxaparin once daily and a minimal change in the use of UFH 3 times daily. Since the pharmacy-driven education program did not differentiate between these options in terms of efficacy, this difference is based on clinician preference and convenience. It might be expected that the use of UFH 3 times daily would have been higher because of its lower acquisition cost compared with LMWH. On the other hand, VTE prophylaxis with LMWH offers several advantages over UFH 3 times daily. The pharmacologic profile of LMWH is superior to UFH, providing a more consistent and predictable anticoagulant response.[32] Some, but not all, of the clinical trials comparing the 2 regimens in medically ill patients suggest better efficacy with enoxaparin 40 mg once daily over UFH 3 times daily.[30,31] The use of LMWH also has a preferred safety profile with less bleeding and less heparin-induced thrombocytopenia compared with UFH.[29-32] Finally, a once-daily SC LMWH injection has more convenient dosing for patients and nurses compared with a 3-times-a-day regimen of UFH. In terms of nursing time, there may be a cost advantage of a once-daily SC injection over a 3-times-a-day regimen.

While our pharmacy education program was associated with improved VTE prophylaxis rates at our institution, we believe further improvements are possible. The clinical pharmacy department has developed and implemented a point-based VTE risk assessment form that will be included in our standard admission packet. This risk assessment form will be completed by nurses and verified by physicians. The VTE risks have been divided into a 5-point system based upon the severity of each risk factor. The cumulative VTE risk score will then be used to determine an appropriate prophylactic strategy. Placement of this VTE risk assessment form in patient charts will be accompanied by additional hospital education. The clinical pharmacy department will review the initial program objectives as well as provide instruction for the risk assessment form. We believe that this 2-pronged approach to VTE prophylaxis, consisting of general VTE education and a patient-specific assessment, can further improve the quantity and quality of VTE prophylaxis at our institution.

Limitations

The foremost limitation of this study was the absence of a control group. Therefore, we cannot fully attribute the changes in quantity and quality of VTE prophylaxis solely to the educational program intervention. When implementing an institution-wide program, it is difficult to have a coincident control group that is not influenced by the intervention program. Therefore, we choose to use a historical control (preeducation) group to measure the results of the intervention program. While historical comparison groups do have the limitation of not being able to control for other possible influences on the outcome being measured, they have been the main study design for trials evaluating clinical pathways.[33-37]

Since there was no control group in the present study, it is possible that other factors contributed to these study findings. However, the time periods for data collection in this study are important since information on the importance of VTE prophylaxis in medically ill patients had already been available. The MEDENOX trial was published in 1999, which was almost 2 years before the start of the in the preeducation period in the present study.[6] The ACCP 6th Consensus Conference on Antithrombotic therapy, which specifically addressed the importance of VTE prophylaxis in medically ill patients, was published in early 2001,[14] about one year before the initial data collection in the present study. Despite this information being available for a significant period of time before the preeducation period of the present study, the utilization of VTE prophylaxis was still low in the preeducation period.

The second most important limitation is that this was a

study of care processes not care outcomes. We did not collect data on either the incidence of VTE in the patients in our institution or the clinical outcomes for patients who did or did not receive VTE prophylaxis. Most clinical trials of VTE in medically ill patients employ contrast venography for the identification of VTE. Since venography is not commonly used in clinical practice, many more patients would be needed to demonstrate differences in symptomatic VTE. It can be argued that it is not necessary to demonstrate a difference in the rate of VTE for there to be success of our pharmacy-driven education program. Clinical trials in several different patient populations have already demonstrated the efficacy and importance of providing VTE prophylaxis.[1] Therefore, improving the utilization of VTE prophylaxis is an appropriate end point in a study of this size.

A third limitation was the retrospective collection of data. It was also not possible to measure the effects of any one component of the educational intervention program since several education methods were used. While we believe the educational presentations to nurses, pharmacists, and physicians and the presence of clinical pharmacists on patient-care rounds had the largest impact, we have no way of making that conclusion definitively.

Fourth, we did not address the patients' smoking status as a risk factor for VTE. Smoking status was newly identified as a risk factor for VTE in the most recent publication of the ACCP Consensus Conference on Antithrombotic Therapy in 2004.[1] This publication was made available in September 2004, after the data collection period for this study. Despite this fact, we do not believe that there would have been significant differences between the groups for this risk factor since there were no statistically significant differences for any other VTE risk factor collected.

We also did not measure administrative costs of the educational interventions or the cost outcomes of VTEs or avoided VTEs in our institution. In a recent article in this *Journal,* Bullano et al. reported a prevalence of VTE of 2.04 per 100,000 study-eligible health plan members. For the incident hospital VTE events, average costs were $7,712 ± $18,339 (median, $3,131) per incident DVT event, $9,566 ± $13,512 (median, $6,424) per PE event, and $12,200 ± $24,038 (median, $6,678) per incident DVT+PE event.[38]

Conclusions

Our pharmacy-driven educational program was associated with a significant improvement in the quantity of use of all 3 categories (any, suitable, and optimal) of VTE prophylaxis. The quality of VTE prophylaxis was also improved, with less UFH twice daily, and more utilization of UFH 3 times daily or once daily LMWH. Institutions implementing a comprehensive educational program may derive more value from measuring changes in both quantity and quality of VTE prophylaxis.

DISCLOSURES

No outside funding supported this study. This paper was presented in part as a poster at the American College of Clinical Pharmacy (ACCP) Annual Meeting in Dallas, Texas, on Tuesday, October 26, 2004. Author Paul P. Dobesh discloses that he is a consultant to sanofi-aventis, the manufacturer of enoxaparin. Author Zachary A. Stacy discloses no potential bias or conflict of interest relating to this article. Dobesh served as principal author of the study. Study concept and design were contributed primarily by Dobesh, with input from Stacy. Data collection was the work of Stacy, with input from Dobesh; data interpretation was the work of both authors. Drafting of the manuscript and its critical revision was the work of both authors.

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