Cost Analysis Before and After Implementation Of a Computerized Physician Order Entry Order Form for Enoxaparin

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ABSTRACT

Objective: The authors sought to analyze the impact of a computerized physician order entry (CPOE) order form for enoxaparin sodium injection (Lovenox) to reduce the daily cost of drug therapy by switching appropriate patients to once-daily enoxaparin administration.

Methods: The study population included patients older than 18 years of age who had been treated with enoxaparin from September 1 to December 31, 2008 (the pre–order form implementation group) and from March 1 to June 30, 2009 (the post–order form implementation group). The wholesale acquisition cost was used to determine the cost of enoxaparin per day. Appropriate dosing was established by chart review.

Results: The post-implementation group showed a trend toward a higher cost of enoxaparin therapy per day compared with the pre-implementation group (P = 0.23). There was a nonsignificant increase in appropriate dosing after implementation of the order form—from 64.5% before implementation to 71.5% after implementation (P = 0.13). In the overall cohort, although the authors controlled for other factors that could influence cost, patients who received the appropriate dose per protocol were 3.2 times more likely (95% confidence interval, 1.8–5.9; P = 0.001) to have lower enoxaparin drug costs per day of therapy.

Conclusion: The use of a CPOE enoxaparin order form did not reduce the daily cost of therapy.

INTRODUCTION

The clinical equivalence of once-daily and twice-daily dosing of low-molecular-weight heparin (LMWH) for the treatment of venous thromboembolic disease has been well established.1–5 Current clinical practice guidelines from the American College of Chest Physicians recommend once-daily or twice-daily LMWH for the treatment of deep vein thrombosis (DVT).6 Merli et al. conducted a randomized, controlled study to compare once-daily and twice-daily enoxaparin sodium injection (Lovenox, Sanofi) with each other, and both enoxaparin regimens with unfractionated heparin UFH), in patients with venous thromboembolic disease.1 The results showed no statistically significant differences in the recurrence of venous thromboembolism (VTE) or in the incidence of major bleeding between any of the three treatment groups.

A subgroup analysis found that cancer and symptomatic pulmonary embolism were significant risk factors for the recurrence of VTE. Patients with obesity or cancer who received once-daily enoxaparin experienced a higher rate of recurrence of VTE than those receiving twice-daily dosing.

Computerized physician order entry (CPOE) and computerized decision support have been used to control the use of diagnostic tests, medications, and other medical resources.7–10 The use of CPOE order forms, in conjunction with integrated decision support, is intended to curtail inappropriate prescribing of medications and to guide physicians in the selection of cost-effective treatments.11,12 During this current era of increased focus on cost containment in health care, it is important to capitalize on potential cost-saving opportunities.

OBJECTIVE

An internal cost analysis at the University of Michigan Hospitals and Health Centers indicated that significant cost savings (almost $100,000 annually), based on enoxaparin-use data, could be achieved by guiding ordering clinicians to select once-daily enoxaparin (1.5 mg/kg) instead of twice-daily dosing for appropriate patient populations. Because these dosing strategies are clinically equivalent, except in certain patients, guidelines for enoxaparin dosing were developed at the institution prior to order form implementation.

The guidelines specify which patient populations should not receive once-daily enoxaparin (1.5 mg/kg), according to the literature, specifically those with active cancer, symptomatic pulmonary embolism, obesity (i.e., weight above 150 kg), or a mechanical heart valve; pregnant patients; and patients being treated for acute coronary syndrome (ACS).13 Patients with severe renal impairment, defined as a creatinine clearance (CrCl) of below 30 mL/minute, as calculated by the Cockcroft–Gault equation, are eligible to receive enoxaparin 1 mg/kg once daily.14 An order form was designed in the CPOE system (Sunrise Clinical Manager XA, version 4.5; Eclipsys Corp.) to help

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ordering clinicians select the most appropriate enoxaparin dosing regimens at the University of Michigan Health System. The CPOE system interfaces with the pharmacy system, where order verification occurs, and the verification is sent back to the CPOE system. The CPOE system is integrated with the medication administration record (MAR).

The order set asks the prescribing clinician seven “yes or no” questions about the patient to determine whether the patient is eligible to receive once-daily enoxaparin (Figure 1):

- Is the patient’s CrCl below 30 mL/minute?
- Does the patient weigh more than 150 kg?
- Does the patient have a mechanical heart valve?
- Is the patient receiving therapy for hemodynamically unstable pulmonary embolism?
- Is the patient receiving therapy for ACS?
- Is the patient pregnant?

If the ordering clinician answers “yes” to any of these questions, the patient is not a candidate for once-daily enoxaparin dosing, and subcutaneous (SQ) enoxaparin 1 mg/kg twice daily is automatically populated in the order form.

If the ordering clinician answers “no” to all questions, the patient is appropriate for once-daily enoxaparin; in this case, SQ enoxaparin 1.5 mg/kg daily is automatically populated in the order form.

If the CPOE system is able to calculate the patient’s CrCl, based on the availability of serum creatinine; the patient’s weight (ideal body weight, unless it is less than actual body weight); and the patient’s height—or if the question regarding the presence of CrCl below 30 mL/minute is answered “yes”—a dose of 1 mg/kg daily is automatically populated in the order form.

A schematic of the decision algorithm that operates in the background of the order form is illustrated in Figure 2 (see page 109). The enoxaparin dose is rounded automatically to the nearest syringe size according to the approved dose-rounding protocol via another algorithm, which is also run in the background. The prescribing clinician has the option of manually changing the order before submitting it.

The CPOE enoxaparin order form was implemented on January 28, 2009. Before the implementation of this form, enoxaparin had been ordered through the CPOE system as a regular order without dosing guidance. The CPOE order form helps the prescribing clinician select the least costly and most appropriate dose of enoxaparin according to the hospital’s protocol. It was hypothesized that the use of the CPOE order form would result in cost savings to the University of Michigan Health System.

Figure 1  CPOE order form for enoxaparin. ACS = acute coronary syndrome; CrCl = creatinine clearance; PE = pulmonary embolism; UH = University Hospital.
METHODS

Our single-center, retrospective study was designed to determine the financial effect of a CPOE enoxaparin order form, upon implementation, in reducing the cost of enoxaparin and to guide ordering clinicians in selecting the most appropriate dosing strategy according to the hospital’s protocol. The study’s secondary aim was to determine whether patients were receiving the appropriate enoxaparin dosing strategy after the order form was implemented. This study was approved by the institutional review board.

Patients who received an enoxaparin regimen of 1 mg/kg once daily, 1.5 mg/kg once daily, or 1 mg/kg twice daily during an inpatient admission and who were older than 18 years of age were enrolled in the study. Patients younger than 18 years of age and those receiving enoxaparin for prophylaxis of DVT were excluded.

The pre-implementation group included patients who had received an enoxaparin-dosing regimen from September 1 to December 31, 2008. The post-implementation group included patients who had received an enoxaparin regimen from March 1 to June 30, 2009. The study design included a washout period before and after the implementation date. A total of 200 patients in each of the two (pre-implementation and post-implementation) study groups were matched based on their medical service and their weight (±5 kg).

Patients’ electronic medical records (EMRs) provided the following data:

- key demographic characteristics (age, sex, height, and weight)
- clinical information (date of admission; admitting service; serum creatinine level; and presence of a mechanical heart valve, cancer, unstable pulmonary embolism, acute coronary syndrome, or pregnancy)
- enoxaparin usage (duration of therapy, dose, frequency of dosing, and the number of doses administered)
- physician responses to the questions on the order form

One of our investigators (R.S.P.) collected the data.

We determined the financial effect of the order form by obtaining the cost of enoxaparin per day of therapy. We calculated this cost using the wholesale acquisition cost during the study, multiplied by the number of doses administered to the patient. We then divided the result by the number of days during which the patient received enoxaparin.

“Appropriate dosing” was defined as enoxaparin 1.5 mg/kg once daily in patients who qualified for once-daily dosing per protocol and as 1 mg/kg twice daily in patients who qualified for twice-daily dosing. If the CrCl was below 30 mL/minute, the appropriate dosage was defined as 1 mg/kg once daily.

Appropriate dosing for the pre-implementation group was determined by the investigator (R.S.P.), who reviewed the patients’ charts and answered the seven questions on the order form. In the post-implementation group, the ordering clinician’s responses to the questions were used to determine appropriate dosing. The investigator verified these responses with a chart review.

We used descriptive statistics to report baseline characteristics and information about hospitalization in the study population. Student’s t-test was used for the continuous variables (age, weight, height, and serum creatinine level), and a chi-squared or Fisher’s exact test was used to compare dichotomous variables (the appropriate dosing strategy per protocol, stratified by costs greater than or less than the median cost per day).

We created a logistic regression model to assess the daily cost of enoxaparin based on the appropriate dosing strategy while adjusting for other factors that predicted cost. To detect a 20% difference in cost between the pre-implementation and post-implementation groups with greater than 90% power and an alpha of 0.05, we had to enroll 400 patients.

A total of 702 patients who received enoxaparin during the pre-implementation period and 812 patients who received enoxaparin during the post-implementation period were identified in the pharmacy database, and 200 patients were randomly matched in each group. The collected cost data were not normally distributed; therefore, we used the median value of
RESULTS

Baseline demographic characteristics were similar between the pre-implementation and post-implementation patient groups except for serum creatinine concentrations (Table 1). The post-implementation group showed a trend toward a higher cost per day of enoxaparin compared with the pre-implementation group; 56.5% and 50.1% of patients, respectively, had a cost per day of $107.55 or higher ($P = 0.23$).

The CPOE order form guided prescribing clinicians in selecting an appropriate enoxaparin treatment regimen and increased the rate of appropriate dosing from 64.5% before implementation to 71.5% after implementation. However, this difference was not statistically significant ($P = 0.13$).

Figure 3 illustrates the number of patients in each group who received appropriate and inappropriate enoxaparin dosing. Fewer post-implementation patients received inappropriate once-daily dosing, with a corresponding increase in appropriate twice-daily dosing.

DISCUSSION

In our study population, the use of a CPOE order form for enoxaparin did not reduce the daily cost of therapy. There was a trend toward a greater number of patients receiving appropriate twice-daily enoxaparin during the post-implementation period than during the pre-implementation period, and there was also a corresponding decrease in inappropriate once-daily, post-implementation dosing; however, these differences were not statistically significant. These findings suggest that patients were receiving inappropriate daily pre-implementation dosing and were switched to appropriate twice-daily dosing in the post-implementation period as a consequence of the CPOE order form criteria. Because twice-daily dosing is more costly, drug costs increased; however, patients continued to receive enoxaparin according to the hospital’s protocol.

Several studies on the use of CPOE and decision support in increasing adherence to treatment protocols have reported positive and statistically significant results in favor of CPOE. By contrast, our own results suggest that decision support within CPOE was unable to uniformly bring about changes in physicians’ prescribing of enoxaparin. The 71.5% rate of adherence to the protocol, after the implementation of CPOE, was directly affected by the ability of ordering clinicians to change the prepopulated enoxaparin regimen before sub-

![Figure 3](image-url)

Figure 3. Number (percent) of patients receiving appropriate and inappropriate enoxaparin dosing before and after implementation of a CPOE order form. Data are presented as n (%).
mitting the order, which allowed them to prescribe outside of the hospital protocol. Ordering clinicians might have changed the dose because of preconceived ideas about enoxaparin dosages or because of a lack of familiarity with the protocol. The pharmacist who verified the orders was not notified that the ordering clinician had changed the prepopulated doses; therefore, no interventions were initiated.

Although cost savings were not realized in the post-implementation group, we examined the potential for savings as if the protocol had been fully utilized. After combining the entire study population (pre-order and post-order sets) and stratifying patients based on appropriate and inappropriate enoxaparin dosing, we found that patients who received appropriate dosing had a lower cost per day of therapy compared with patients who received inappropriate dosing.

The cost per day of therapy with enoxaparin was $107.55 or more in 45.9% and 69.5% of the two groups, respectively ($P < 0.001). This difference remained statistically significant even after patients with a CrCl below 30 mL/minute were excluded. Moreover, patients who received the appropriate enoxaparin regimen per protocol were 3.2 times more likely (65% CI, 1.8–5.9; $P = 0.001) to have a lower enoxaparin drug cost per day of therapy compared with patients who received inappropriate dosing after adjustments were made for weight and CrCl values.

To realize the potential cost savings that were seen with dosing according to protocol, the enoxaparin order set will be programmed to prevent ordering clinicians from changing the prepopulated enoxaparin dose before submission of the order. If the ordering clinicians still want to change the dose, they will be required to contact a pharmacist for evaluation. The pharmacist has the ability to order a non-protocol dose after assessment of the patient if such a dose is warranted.

**STUDY LIMITATIONS**

As with any retrospective analysis, our study had several potential limitations, including missing or inaccurate data (i.e., laboratory values and cancer history), investigator bias, and allocation bias with noncomparable groups. However, the amount of inaccurate data is likely to be small, and given the sample size, such data would be expected to have a minimal effect on the study’s conclusions. In an effort to remove investigator bias, we defined all outcomes and predictors using objective, standardized criteria before the start of the study. In addition, we rigorously defined the study protocol for the collection of all data sets to ensure uniformity.

**CONCLUSION**

In our study, the CPOE enoxaparin order form did not bring about reductions in the daily cost of therapy. However, significant cost savings resulted when patients received enoxaparin according to hospital protocol. These cost savings persisted even after adjustments were made for weight and CrCl. The full potential for cost savings with the hospital’s protocol was not realized after the implementation of the CPOE order form. Changes to the order form and oversight by a pharmacist should help the institution achieve these cost savings.

**REFERENCES**


