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Consumption Pattern of Enoxaparin in a Non-teaching Hospital

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ABSTRACT

Background: Drug use evaluation studies are conducted to assess the pattern of prescribing and administration of a drug. Deep vein thrombosis is one of the most important clinical issues around the world. This study examined the pattern of enoxaparin consumption, one of the most widely used anticoagulant, for prevention and treatment of thrombosis in a non-teaching hospital.

Methods: In this cross-sectional prospective study, 117 patients receiving enoxaparin in different wards of Imam Sajjad Hospital in Ramsar, Iran were studied. Data on how to prescribe and use of enoxaparin were recorded in a questionnaire designed according to UpToDate recommendations. Demographic variables, prophylaxis and therapeutic indications, prophylaxis and treatment doses, interval and monitoring information were evaluated. Finally, the results were compared with UpToDate suggestions.

Results: The mean age of patients was 68.9 years and 52.1% of them were men. Enoxaparin was prescribed for 35.9% of patients as prophylaxis and 64.1% of patients received this drug for the treatment. Overall, prophylactic doses were inappropriately administered in 41.5% of patients. Improper therapeutic doses were also prescribed for 52% of subjects.

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Conclusion: The results of this study showed that in terms of the dosage and interval of enoxaparin administration were significantly inappropriate. It seems, the prescribers must have more adherence to the valid and reliable enoxaparin guidelines for more rational practices.

Keywords: LMWH, DUE, Enoxaparin, Hypertension, Appropriate.

Introduction

Drug utilization evaluation (DUE) is an authorized, structured, ongoing study that examines how a drug is prescribed and administered. (1) This method is especially important for drugs with narrow therapeutic index, high price, major side effects, and special-uses. Rational use of drugs is important because the overuse of drugs, low consumption or misuse of them cause to waste of resources or considerable harm to the health of people.(2) Anticoagulants are used in numerous situations as an earliest medical interventions to treat acute venous thromboembolism (VTE), atrial fibrillation (AF), and acute coronary syndrome in patients undergoing cardiovascular or peripheral vascular surgery and is used in the early stages of treating myocardial infarction, a heart attack or stable angina. These drugs can be administered for prophylaxis of VTE in critically ill patients or with artificial valves, AF and post operation cases.(3)

Unfractionated heparin (UFH) as well as low molecular weight heparin (LMWH) such as enoxaparin, are important anticoagulants that are especially used for when requiring rapid anticoagulant effects.(4) LMWHs have some benefits compare to heparin such as more bioavailability, higher predictable dose response, available at fixed doses, no need regular monitoring and less common thrombocytopenia.(5, 6) The main purpose of this study was to evaluate consumption of enoxaparin (in terms of dosage, interval, necessary monitoring) in a non-teaching hospital.

Materials and Method

This cross-sectional prospective study was performed in patients referred to the Imam Sajjad Hospital in Ramsar, north of Iran. All patients who were admitted to internal, cardiac, coronary care unit, and surgery departments and received enoxaparin were enrolled in the study and data were collected during 12-months, from October 2018 to September 2019. There wasn't a predetermined criterion for excluding the patient from the study. The data collection tool was a questionnaire that designed based on UpToDate instruction. Patients' clinical information was collected on the basis of the indicators designed in the questionnaire, through records in the wards, as well as face to face interviews with patients, physicians and trained staff. Demographic information including age, gender, height and weight, as well as inpatient ward, diagnosis, drug history, past medical history were also been considered. The dose of prophylaxis or treatment and laboratory variables affecting the efficacy or side effects of enoxaparin including the number of platelets, serum potassium, serum creatinine (Cr) and blood urea nitrogen (BUN) levels, partial prothrombin time (PPT), international normalized ratio (INR) and complete blood counts (CBC) were assessed before, during and after enoxaparin administration.

Data analysis

SPSS 24 software was used for data analysis and chi-square test was used for qualitative variables and P value <0/05 was considered as significant difference.

Results

Totally the pattern of enoxaparin administration in 117 patients were reviewed. The average age of the participants was 68.91 (37-93) years and 56 subjects (47.9%) were women and 61 (52.1%) of them were men. None of women were pregnant. Reasons for hospitalization were cardiovascular (53%), neurological (16.2%), respiratory diseases (10.4%), DVT (5.1%), respiratory disease (10.4%), electrolyte abnormalities (3.4%), gastrointestinal diseases (2.6%), kidney diseases (2.6%), cancer (2.6%), infection (2.6%), poisoning (0.9%) and blood disorders (0.9%).

Cardiologists prescribed enoxaparin for the majority (47.9%) of patients and followed by internal diseases specialists (33.3%), infectious diseases specialists (12%) and neurologists (6.8%).

Thirty-one subjects (35.9% of all) were received enoxaparin for prophylaxis purposes. The most common indication for prophylaxis was inability to move due to acute illnesses (table 1).

Non-ST-elevation myocardial infarction (NSTEMI) was the most frequent therapeutic indication (64% of patients) for enoxaparin consumption. DVT, ischemic stroke, ST-elevation myocardial infarction (STEMI), transient ischemic attack (TIA) and percutaneous coronary intervention (PCI) were other indications, respectively (table 2).

Although all patients received enoxaparin for the purpose of preventing DVT medical patients with acute illness at appropriate intervals, the drug was prescribed to 41.5% of patients with incorrect doses (table 3). At the point of therapeutic view, 50% of the patients with NSTEMI received this medicine with an inappropriate dose and 37.5% received at improper intervals. Enoxaparin was incorrectly prescribed in the majority of patients with DVT, ischemic stroke or STEMI considering doses and intervals (table 3). Totally, therapeutic doses were ordered for 52% of patients with inappropriate doses.

At the beginning of enoxaparin consumption CBC, BUN and Cr were monitored for all patients. At the baseline, 13 patients (11.1%) had creatinine clearance less than 30 mL/min/1.72m2 and they received usual dose the same as other cases with normal kidney function. Also 3 patients (2.6%) had platelet count less than 100.000/mcL (75.000, 56.000 and 28.000) while enoxaparin prescribed for them. Also, during treatment, the platelet counts of two patients (1.7%) decreased more than 50%, but medication continued for them at the usual manner.

Discussion

In this cross-sectional study in which a total of 117 hospitalized patients were received enoxaparin in different wards of a non-teaching hospital were evaluated. The results showed that in patients with inability to move due to acute illnesses (the most popular indication for prophylaxis), the prescribed doses for DVT prevention were proper only in 58.5% of patients (41.5% received improper doses), however all patients (100%) received the drug at appropriate intervals. In patients under treatment, enoxaparin was incorrectly prescribed in the remarkable of patients with NSTEMI (50% & 37.5%), DVT (33.3% & 11.1%), ischemic stroke (47.4% & 15.4%) or STEMI (50% & 0%) considering doses and intervals, respectively.

Similar to the present study, Hassani et al. mentioned that 20.45% of prophylactic doses of enoxaparin were compatible with published guidelines and 79.55% of patients received higher doses than recommended. For therapeutic purposes, 57.27% of patients received correct recommended doses of enoxaparin and 40.6% and 2.13% of subjects received more or less doses, respectively.(7)

Enoxaparin for prophylaxis or treatment was reviewed by Khalili et al. considering 4 fixed parameters including definite indication, correct dose, monitoring and treatment duration. In this study enoxaparin was prescribed 82% appropriately and 18% of cases inappropriately. Also, 21% of patients were received improper doses of enoxaparin.(8)

Similarly, Fahimi et al. reported that enoxaparin was improperly administered in 53.74% and 75.51% of patients in the terms of dose and duration, respectively.(9) Alike to our study, 57.3% of patients in the study by Emadian et al that received enoxaparin as prophylactic doses were not matched with recommended value.(10)

In the study of Chung et al. none of aspects of dose, interval, duration and time of the first dose of enoxaparin were compliant to NUH guideline.(11) Nekoonam et al. showed 73.33% of subjects received correct doses of enoxaparin and totally 26.67% of this prescribed anticoagulant were incorrect.(12) Eslami et al. reported that accordance rate of enoxaparin dosing with the valid guideline was 81.5% in patients at a teaching hospital.(13) Zeitoun et al was observed inappropriate regimen of enoxaparin in 40.2% of patients mostly for VTE prevention and for the treatment of USA/NSTEMI and VTE, respectively.(14) Our study and several other researches show that despite the availability of valid guidelines and emphasis on the rational use of enoxaparin, many doctors in numerous centers do not have adherence these guidelines enough.

Monitoring of patients before and during treatment

In the present study, although 11.1% of patients had reduced kidney function with creatinine clearance less than 30 mL/min/1.72m2, the standard doses of enoxaparin were ordered for them. It has been shown that in patients with reduced kidney function, the use of the usual dose of enoxaparin increases the level of anti-Xa and the risk of bleeding.(15) Fahimi et al. mentioned that 5.3% of patients had ClCr less than 30 ml/min and proper dosage adjustment was only performed for half of patients.(9) In addition, in Zeitoun et al study 88.64% of patients with CrCl <30 ml/min did not receive the suitable doses.(14) In the study by Hassani, none of the 3 patients whose had GFR less than 30 ml/min received the appropriate dose.(7) Therefore, it seems that clinicians should make more efforts to use adjusted dose of enoxaparin in patients with impaired renal function to

reduce the risk of side effects. Although the guideline panel of American Society of Hematology (ASH) don't recommend using anti–factor Xa concentration monitoring for enoxaparin dose adjustment in patients with creatinine clearance less than 30 mL/min, considering product labeling to use proper doses based on renal function or changing to another anticoagulant with lower renal clearance (such as unfractionated heparin) are suggested.(16)

Considering that thrombocytopenia is a significant side effects of enoxaparin, checking of platelet count at baseline, repeat within 24 hr, then every-other-day from day 4 to 14 is recommended.(17) If the initial platelet count is less than 100.000/mm3 or decrease more than 50% of the initial value during the treatment, enoxaparin therapy should be discontinued and alternative therapy advised. In our study, at the beginning of therapy, 3 patients had a platelet count less than 100.000/mm3 while the treatment with usual dose of enoxaparin was initiated and platelet monitoring was performed only for one of the 3 patients during the treatment. Also, the platelets count decreased in 2 patients by more than 50% during the treatment but the medication consumption continued at the usual manner for them.

Thrombocytopenia was observed in 2.8% of patients in the study of Zeitoun et al., and platelet count was not requested for 3.4% and 23.9% of patients at the beginning and during treatment, respectively.(14) In some studies, platelet count monitoring has been better. Emadian et al reported that platelet monitoring was done for all of patients at baseline and 98% of them during the study at the teaching hospital.(10)

Conclusion

The results of our study showed that the doses and intervals of enoxaparin were not appropriate in the different specialty disciplines for various indications. It seems that enoxaparin prescribers need more adherence to the valid guidelines and authentic therapeutic resources to treat patients more accurately.

Ethical Considerations

Compliance with ethical guidelines

The Research Committee of the Mazandaran University of Medical Sciences, Sari, Iran approved this study (Protocol no. IR.MAZUMS.REC.1396.10237).

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Conflicting interests

All authors declare no potential conflicts of interest for conducting the study and publishing the article.

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Authors' contributions

Conceptualization, Mohammadreza Rafati, Shahram Ala; Methodology, Mohammadreza Rafati, Mahsa Heydari; Investigation, Mahsa Heydari, Bita Lashto-Aghaee; Writing – Original Draft, Mahsa Heydari, Bita Lashto-Aghaee; Writing-Review & Editing, Mohammadreza Rafati, Shahram Ala; Supervision, Mohammadreza Rafati; All authors contributed to obtain final approval.

Tables

Table 1. Administration of enoxaparin aim to DVT prophylaxis

Prophylaxis Indications	Female	Male	Total
Medical patients with acute illness	17	24	41
Abdominal surgery patients	1	0	1
Total	18	24	42

Table 2. Use of enoxaparin for therapeutic indications

Therapeutic Indications	Female	Male	Total
NSTEMI	27	21	48
Deep vein thrombosis	5	4	9
Ischemic stroke & TIA	5	6	11
STEMI	2	2	4
TIA	0	2	2
PCI	0	1	1
Total	39	36	75

Table 3. Appropriateness of enoxaparin administration for prophylactic and therapeutic indications

Indication			Proper consuming patients/total patients No (%)	Improper consuming patients/total patients No (%)
DVT Prophylaxis	Medical patients with acute illness and	Dose	24/41 (58.5%)	17/41 (41.5%)
		Interval	41/41 (100%)	-
	Abdominal surgery	Dose	1/1 (100%)	-
		Interval	1/1 (100%)	-
Therapeutic	NSTEMI	Dose	24/48 (50%)	24/48 (50%)
		Interval	30/48 (62.5%)	18/48 (37.5%)
	DVT	Dose	6/9 (66.7%)	3/7 (33.3%)
		Interval	8/9 (88.9%)	1/9 (11.1%)
	Ischemic stroke & TIA	Dose	6/13 (42.6%)	7/13 (47.4)
		Interval	11/13 (84.6%)	2/13 (15.4%)
	STEMI	Dose	2/4 (50%)	2/4 (50%)
		Interval	4/4 (100%)	-
	PCI	Dose	1/1 (100%)	-
		Interval	1/1 (100%)	-

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