Brief Communication

Evaluation of Venous Thromboembolic Event Prophylaxis in Hospitalized Cancer Patients: A Single-Centered Retrospective Study

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ABSTRACT

Objective: Venous thromboembolic events (VTEs) are one of the main causes of death in cancer patients. About one-third of newly diagnosed VTEs are later proved to be associated with cancers. Attempts have been made to prevent these events and reduce substantial burden on patient health. Previous studies have revealed underutilization of thromboprophylaxis in cancer patients. With respect to the high rate of enoxaparin prescription in our institute, irrational utilization of prophylactic measures was anticipated. This study aimed to evaluate the appropriateness of thromboprophylaxis in hospitalized cancer patients. **Methods:** Medical records of 199 cancer patients hospitalized in two oncology wards of a tertiary care teaching hospital were investigated retrospectively. Data extraction was performed by two clinical pharmacists. Appropriateness of thromboprophylaxis was determined using a local protocol prepared based on international guidelines. **Findings:** Forty-seven out of 199 prescriptions (23.5%) were appropriate according to the local protocol. About 76% (149/199) of patients did not have any acute medical illness or risk factors for thromboembolism and were admitted only to receive short-course chemotherapy. Enoxaparin was the drug used for 197 patients and unfractionated heparin was used for only 2 patients. Dose adjustment was not performed in three patients who needed dose modification with respect to renal impairment or obesity. **Conclusion:** This study has found that the frequency of thromboprophylaxis was considerably high in the study population. In the absence of an acute medical illness or other risk factors, hospitalization *per se* does not justify the administration of pharmacologic agents for thromboembolism prophylaxis. Implementation of local protocols prepared based on international guidelines seems necessary to rationalize thromboprophylaxis.

Keywords: *Cancer, Enoxaparin, overutilization, prophylaxis, thromboembolism*

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Introduction

Venous thromboembolic events (VTEs) are the second leading cause of mortality in cancer patients.[1] Patients with malignant disorders are in a hypercoagulable state, rendering them prone to VTE. The relationship between cancer and VTE has widely been appreciated, which is reflected by up to 6.5 times higher incidence of VTE in cancer patients compared with other patients.[2] New findings suggest that approximately 20%–30% of newly diagnosed VTEs are associated with cancers.[3]

A number of factors have been known to be correlated with an increased risk of VTE in this population. Risk factors associated with tumor include tumor entity, location, stage, and the time since diagnosis. Patient-related factors such as advanced age, obesity, the presence of comorbidities, history of thrombotic events, and inherited thrombophilias may potentiate the risk of VTE in these patients. The risk could also be affected by the chemotherapy regimen.[4]

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Compared with other patient populations, the risk of recurrent VTE and bleeding is higher in patients with malignancy, which results in a higher rate of hospital admission and considerable financial burden on the health-care system. The occurrence of VTE not only imposes considerable cost but also adversely affects morbidity and patient outcome.[5] Results of a large-scale survey on surgeons and medical oncologists revealed that routine thromboprophylaxis was used by about 50% of surgeons and only 5% of medical oncologists,[6] which indicates underutilization of pharmacologic thromboprophylaxis in this high-risk population.

With respect to unfavorable health outcomes associated with VTE, some practitioners may be inversely motivated toward the irrational use of prophylactic methods, which in turn imposes additional risks and costs on patients. Adherence to guidelines prepared by authoritative organizations could prevent the inter-practitioner difference in patient management.

Data extracted from our hospital information system revealed that nearly all patients admitted to oncology wards received anticoagulants in prophylactic doses. With respect to the magnitude of anticoagulant use, overutilization of VTE prophylaxis was suspected. The aim of this study was to evaluate the appropriateness of VTE prophylaxis in a population of cancer patients admitted to a tertiary care hospital.

Methods

This was a retrospective study conducted on medical records of patients admitted to two oncology wards of a tertiary care teaching hospital in Tehran, Iran. Medical records of 196 cancer patients who received pharmacologic VTE prophylaxis and hospitalized from March to June 2017 were selected using convenience sampling method. Data extraction was performed by two clinical pharmacists (Sholeh Ebrahimpour and Mehdi Mohammadi). Patients' demographic data, past medical history, laboratory tests, body mass index, drug history, and dose and duration of VTE prophylactic medication were recorded.

Eligibility criteria for VTE prophylaxis and dose/duration of anticoagulants were determined by a panel consisting of oncologists and clinical pharmacists based on recommendations extracted from the National Comprehensive Cancer Network,[7] the American Society of Clinical Oncology,[8] and the International Society on Thrombosis and Haemostasis[9] clinical practice guidelines on venous thromboembolic prophylaxis in cancer patients [Table 1].

Anticoagulation for surgery patients was recommended to be initiated before surgery and continued for 7–10 days after surgery.

Descriptive data analysis was performed using SPSS Statistics Software (Version 21.0. IBM Corp., Armonk, NY, USA). The results were reported as numbers and frequencies. The study population was considered as one group, and subgroup analysis was not performed.

Results

Medical records of 199 patients (75 males [37.7%] and 124 females [62.3%]) were investigated. The mean age was 50.6 ± 13.8 years.

VTE prophylaxis was appropriately implemented in 47 patients (23.5%) which included 31 patients with advanced lung or pancreatic cancer, 1 patient with multiple myeloma, 6 patients with acute medical illness, 4 patients with planned surgery, 2 patients with reduced mobility, and 3 patients with a prior history of VTE.

One hundred fifty-two patients (76.4%) received VTE prophylaxis without acute medical illness or any identifiable risk factor for VTE. Almost all of these patients were admitted to receive short-course chemotherapy.

Only 2 patients received unfractionated heparin, and others (197 patients) received enoxaparin as VTE prophylaxis. The medication doses were 5000 IU three times daily for unfractionated heparin and 40 mg once daily for enoxaparin. None of the patients received physical prophylaxis in combination to anticoagulation. Medication dose was inappropriate in 3 (6.4%) eligible patients. Dose adjustment was not performed according to renal impairment in two patients. In addition, the dose was not adjusted in one patient with obesity (body mass index >40 kg/m^2). There were no recorded contraindications to pharmacological VTE prophylaxis in the study population.

The mean duration of receiving prophylactic anticoagulation was 4.1 ± 3.3 days (minimum: 1 day and maximum: 36 days). Ineligible patients totally received 583 doses of enoxaparin which corresponds to 81.6 million IRR.

There was no report of bleeding, hematoma formation, or any serious adverse reaction secondary to heparin or enoxaparin administration.

Discussion

An unanticipated finding of this study was that the majority of patients who received enoxaparin did not fulfill VTE prophylaxis criteria. The findings

Table 1: Institutional panel recommendations for venous thromboembolic event prophylaxis in cancer patients

Indications
Cancer patients hospitalized with an acute medical illness, reduced mobility, or history of VTE*[8]
Patients with locally advanced or metastatic pancreatic cancer undergoing chemotherapy[9]
Patients with locally advanced or metastatic lung cancer undergoing chemotherapy[9]
Cancer patients hospitalized for surgery[8]
Patients with multiple myeloma who have VTE risk factor or receive thalidomide/lenalidomide in combination with chemotherapy (multiagent chemotherapy, doxorubicin, or more than 480-mg dexamethasone in a month)[8]
Patients with Khorana score ≥3 in the outpatient setting[7]
Duration[7,8]
In the context of acute medical illness, anticoagulation should be continued throughout the hospital stay
In multiple myeloma patients, anticoagulation should be considered as long as active treatment is continued
For surgery patients, anticoagulant should be initiated before surgery and continued for 7-10 days
For patients undergoing major abdominal or pelvic surgery with high-risk features†, anticoagulation may be continued for up to 4 weeks
For patients admitted with outpatient Khorana score ≥3, anticoagulation should be initiated/continued as long as the patient is eligible for anticoagulation based on Khorana score
Dose[7]
Enoxaparin
Standard dose: 40 SC daily
Obesity dosing (BMI ≥40 kg/m^2): 40 mg SC every 12 h
Renal insufficiency dosing (CrCl <30 mL/min): SubQ: 30 mg once daily
Unfractionated heparin
5000 units SC every 8-12 h
Obesity dosing (BMI ≥40 kg/m^2): 7500 units SC every 8 h

*Patients admitted to receive short-course chemotherapy or to undergo minor procedures with no risk factor for VTE or acute medical illness were considered ineligible to receive VTE prophylaxis, †Risk factors include age ≥65, metastatic disease, ascites, congestive failure, BMI ≥25 kg/m^2, platelet count >400,000/mL, serum albumin <3 g/dL, duration of surgery >2 h.[10] VTE=Venous thromboembolic events, BMI=Body mass index

of the current study are inconsistent with those of Awar and Sheikh-Taha who found that only 22.1% of qualified patients for VTE prophylaxis received anticoagulation.[11] We found no previous study evaluating the appropriateness of VTE prophylaxis in cancer patients in our population, but the rate of appropriate VTE prophylaxis was relatively higher in the noncancer patient population like patients hospitalized in medical wards or intensive care units.[12,13] Overutilization of VTE prophylaxis in the current study may be justified in part by the misconceptions of guideline recommendations by the practitioners. Almost all patients who received inappropriate VTE prophylaxis in the current study were admitted only to receive the planned course of chemotherapy. In fact, they were not hospitalized because of acute medical illnesses, and there were no additional risk factors for VTE such as reduced mobility, history of VTE, and high-risk tumor types. These patients would be rationally considered as outpatients and their risk for VTE was calculated according to Khorana Predictive Model for Chemotherapy-Associated VTE.[14] The patients who are eligible to receive prophylaxis in the outpatient setting based on Khorana Model can continue anticoagulation during hospitalization for short-course chemotherapy.

The development of local protocols based on the international guidelines by a panel consisted of physicians, and clinical pharmacists seem to improve the rational use of anticoagulants for VTE prophylaxis. These protocols may be later approved and supervised by local drug and therapeutic committees. Such practices have proven effective in previous studies. For example, in a study by Khalili *et al.* which was conducted on patients with infectious diseases, implementation of a locally prepared VTE prophylaxis protocol improved the appropriate prophylaxis from 69.9% to 88.4% of prescriptions.[12] Better results may be achieved by interactive approaches to improve physician contribution and to shed light on possible misconceptions from local protocols.

Although enoxaparin is used at fixed doses for VTE prophylaxis, it must be kept in mind that certain subgroups of patients require dose modifications because of obesity or impaired renal function.[7] In this study, dose modification was considered for none of the patients with such concerns (3 patients).

Another result of the study which deserves attention is the cost imposed by the overutilization of anticoagulants. In addition, it should be noted that the financial burden is not solely related to the direct cost of medication but also to the costs associated with the occurrence

of adverse effects which may lead in prolongation of hospital stay. Although no severe drug-related complication was observed in this study, it may appear on widespread clinical use.

The most important limitation lies in the fact that the study was conducted retrospectively. Therefore, some data may have been missed such as the family history of VTE. Another source of weakness in this study was the sampling method which may have resulted in selection bias, and consequently, the study sample may not have represented our interested population.

What is now needed is a pre- and poststudy to evaluate the effectiveness of interventions aimed at improvement of VTE prophylaxis prescriptions. Further, conducting additional studies targeted at outpatient setting will be helpful.

These findings suggest that the development of local protocols is an essential step to encourage practitioners toward rational VTE prophylaxis utilization.

Authors' Contribution

Zahra Jahangard-Rafsanjani and Sholeh Ebrahimpour contributed to idea development and study design. Mehdi Mohammadi and Sholeh Ebrahimpour performed the data extraction and analysis and prepared the manuscript. All authors read and approved the manuscript.

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Conflicts of interest

There are no conflicts of interest.

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