

Evaluation and improvement of venous thromboembolism prophylaxis pattern in patients admitted to orthopedic ward in a tertiary teaching hospital

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Abstract:

Venous thromboembolism (VTE) includes deep vein thrombosis (DVT) and pulmonary embolism (PE). VTE incidence in major orthopedic surgery ranges from 40% to 60%. Several risk factors are responsible for VTE incidences, such as age, obesity and immobility. This study was designed and performed to evaluate the process of thromboprophylaxis in patients undergoing orthopedic surgery with and without pharmacist intervention to improve prescribing. A total of 306 patients were randomly enrolled in the two phases of this study. To investigate the cause of VTE, 201 patients receiving no pharmacist interference as study phase one and 105 patients receiving pharmacist interference as study phase two were evaluated. Rate of occurrence of risk was calculated using the Caprine scoring system. The trend of prescription and the reasons for not prescribing the drugs under consideration for the patients, were investigated. As a subsidiary aim to the study and to increase economical productivity, the prescription of heparin instead of other anticoagulating drugs was suggested in pharmacotherapy consultation. In the first phase of the research, it was proven that 161 (80.1%) of the patients under consideration needed the prophylaxis but 40 (19.9%) of them did not. After the investigation, 171 (85.1%) of the patients according to the guideline and 30 (14.9%) without considering the guideline underwent prophylaxis. In the second phase of the research, 40 (38.1%) of the patients did not require prophylaxis treatment but 65 (61.9%) did. After investigation and drug interaction results, 96 (91.43%) according to the guideline and 9 without considering the guideline were treated with the prophylaxis drug. Despite the active presence and cooperation of pharmacists, 4.76% who did not need prophylaxis received it, and 6.15% who needed prophylaxis did not receive it despite the pharmacist's intervention. Moreover, 2.86% of patients who were prohibited from taking enoxaparin were allowed to take heparin after pharmacist intervention. This research showed that active cooperation between orthopedist and pharmacist in prescribing the required drug(s) is very low. For this reason, the continuous presence of a pharmaceutical group as well as changes in protocols can serve as an effective, logical step in the prescription of drugs.

Keywords: prophylaxis; venous thromboembolism; orthopedic; heparin; enoxaparin

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1. Introduction

Venous thromboembolism (VTE), which includes deep vein thrombosis (DVT) and pulmonary embolism (PE), is the third most common cardiovascular disorder after myocardial infarction and a major cause of death in hospitalized patients [1, 2]. About 300,000 to 600,000 people in the United States develop VTE each year, and 60,000 to 100,000 American patients die of VTE each year [3].

The risk of developing VTE increases dramatically during surgery, especially in orthopedic surgeries [4,5,6]. Because non-standard methods for preventing VTE lead to consequences such as repeated hospitalizations, exorbitant costs, and mortality, thromboprophylaxis has been identified as a reliable tool for preventing VTE [7]. In fact, not only is accurate prevention of VTE vital, but it is also important to avoid incorrect anticoagulant therapy given the risk of bleeding [8]. According to the 2008 American College of Chest Physicians' (ACCP) recommendations for preventing VTE in the Middle East, only 8-78% of patients in need of prophylaxis receive medication. Moreover, 66% of patients with contraindications for thromboprophylaxis and 78% of patients who do not need thromboprophylaxis receive inappropriate prophylactic treatments [9].

As most cases of VTE can be prevented through appropriate administration of anticoagulants, individual assessment of the risk of thrombosis in patients admitted to the orthopedic ward and the administration of the appropriate anticoagulant drug as prophylaxis are necessary.

Many studies have been conducted in different countries for thromboprophylaxis [10,11,12]. In a study conducted by Krauss et al. (2019) to determine the effectiveness of using Caprini criteria in predicting the occurrence of VTE in patients undergoing arthroplasty, it was found that 7 out of 8 patients with VTE were identified when Caprini criteria were used, and only one case could be identified when it was not [11].

In a meta-analysis conducted by Farfan et al. (2016) to assess adherence to ACCP guidelines for the prevention of thrombosis after major orthopedic surgery, it was found that over time, compliance with ACCP instructions increased during hospitalization but decreased after discharge [12]. Because of the importance of VTE as a dangerous complication in

orthopedic patients, the present study investigated and modified the prevention of thrombosis in patients admitted to the orthopedic ward and the degree of compliance with existing guidelines in this field.

2. Materials & Methods

A total of 306 patients admitted to *Ayatollah Taleghani Educational Hospital in Tehran, Iran*, for orthopedic surgery were randomly enrolled in the current study. Ethics committee approvals were obtained before the initiation of the study. Demographic information regarding age, sex, underlying disease, history of drug use, history of surgery or trauma, Hgb, INR, PTT, PT, CBC, platelet count, creatinine level, and amount of liver enzymes were extracted from patients' medical records.

The risk of thrombosis was calculated and recorded based on Caprini criteria[13] for all subjects, and individuals were divided according to their risk level into four groups of very low, low, medium, and high risk (Table 1).

Two cross-sectional study phases were defined at the same study sites, and data from 201 and 105 patients, respectively, were collected within a 450-day interval.

2.1. First Cross-Sectional Phase

In the cross-sectional study phase (n=201; age (years): $40/05 \pm 17/18$; height (cm): $171/46 \pm 8/59$; weight (kg): $75/33 \pm 14/51$; BMI: $25/59 \pm 4/43$), patients were evaluated for the rational administration of anticoagulants in the orthopedic ward without pharmacist intervention.

2.2. Second Cross-Sectional Phase

In this cross-sectional study phase (n=105; age (years): $40/38 \pm 18/64$; height (cm): $173/23 \pm 9/02$; weight (kg): $75/86 \pm 14/63$; BMI: $25/23 \pm 4/48$), in addition to evaluating the rational prescription of drugs, patients were also reviewed in terms of dosage correction and indications for their use. Patients in this group were given pharmacotherapy counseling for any necessary changes in pharmaceutical intervention, which was then applied at the discretion of the orthopedic resident. All patients were monitored for blood and physiological parameters during hospitalization. Data was analyzed using McNemar test[14] with SPSS-19.

Table 1. Characteristics of the study population

Type of Risk Factors	First Cross Sectional Phase (N=201) n (%)	Second Cross Sectional Phase (N=105) n (%)
Age(years)		
75≤	6(2/98)	6(5/71)
61-74	19(9/45)	8(7/62)
41-60	50(24/87)	26(24/76)
Obesity (BMI > 25 kg/m2)	97(48/26)	40(38/10)
Sex hormone therapy	1(0/50)	1(0/95)
Fractures of the bones of the legs and pelvis	45(22/39)	29(27/62)
Elective arthroplasty surgery	24(11/94)	8(7/62)
Stroke (less than a month)	0(0)	0(0)
VTE history	0(0)	0(0)
VTE family history	0(0)	1(0/95)
Arthroscopic surgery	27(13/43)	10(9/52)
Malignancy	6(2/98)	1(0/95)
Restricted to bed (more than 72 hours)	114(56/72)	18(17/14)
Immobilizing plaster cast	67(33/33)	24(22/86)
Varicose veins	0(0)	0(0)
Taking oral contraceptives or hormone replacement therapy	1(0/50)	1(0/95)
Serious lung disease including pneumonia (less than one month)	1(0/50)	0(0)
Risk of thrombosis		
Very low	0(0)	0(0)
low	0(0)	0(0)
medium	30(14/9)	35(33/3)
high	171(85/1)	70(66/7)

3. Results & Discussion

The results of demographic and contextual information in both phases of the study are shown in Table 1. The highest frequency distribution in terms of age was 41-60 years in both phases of the study. Restriction to the bed for more than 72 hours was the most common cause of hospitalization in first-phase patients (72.56%), and fractures of the leg and pelvic bones were causes of hospitalization in the second-phase patients (27.62%). In both phases, individuals were at high risk for thrombosis.

3.1. Phase I results

The results of the study of patients in phase I were reported in two sections: one subgroup of patients required prophylaxis, while the second subgroup did not. The results of this study showed that out of 201 patients, 161 (80.1%) needed prophylaxis, 152 (75.6%) of whom received enoxaparin as their prescribed medication. Of all patients studied in this phase, 171 (85.1%) were at high risk and 30 (14.9%) were at moderate risk for

thrombosis; 150 (87.7%) high-risk and 21 (70%) moderate-risk patients underwent prophylaxis according to the guidelines.

In a review of 161 patients in need of prophylaxis, 143 (88.8%) received medication, of whom 87% were medicated according to the guidelines.

In the second part of phase I, it was observed that out of 40 patients (19.9%) with no need for prophylaxis, 31 (77.5%) underwent prophylaxis according to the guidelines and received no medication; contrary to the guidelines, 9 (22.5%) patients received medication.

3.2. Phase II results

Out of 105 patients studied in phase 2, 66 (62.9%) received medication. It was also observed that from the 105 patients, 65 (61.9%) required prophylaxis, and 61 (93.8%) of them received medication. The proposed intervention instructions were performed on 10 (16.4%) of the 61 patients according to the guidelines, but 51 (83.6%) patients were treated not in accordance with the guidelines.

It should be noted that the reasons for the intervention were compliance with the guidelines and cost reduction (30% and 70%, respectively).

In the second phase, out of 65 people who needed prophylaxis, 4 (6.2%) did not receive medication. All four individuals were offered pharmacist intervention but refused to receive the drug at the discretion of the treating physician.

The status of prophylaxis compliance with the guidelines after intervention in phase II patients was reported to be 96 (91.4%). Overall, 66 (94.37%) high-risk patients and 30 (85.7%) moderate-risk patients received medication according to the guidelines.

Before the intervention, enoxaparin was administered in 97% of patients, but after the intervention, 85% received enoxaparin and 15% received heparin.

In the second part of Phase II, which aimed to evaluate patients with no need for prophylaxis, the results showed that among 40 patients who did not require prophylaxis, 35 (87.5%) underwent prophylaxis according to the guidelines and 5 (12.5%) did not undergo prophylaxis according to the guidelines. The proposed intervention program with the aim of not prescribing the drug was suggested to all 5 patients who received the drug, and at the discretion of the treating physician, intervention orders were not carried out on these individuals.

The results of the McNemar test showed that there was no significant difference between the proportion of people receiving the drug according to the guidelines in the first and second phases ($p = 0.11$, Table 2). Furthermore, no significant difference was observed in the second phase between the ratio of drug intake according to the guidelines before and after the intervention. Therefore, it can be said that the intervention of receiving medication according to the guidelines was not effective.

Table 2. Evaluation of proportion of people receiving the drug according to the guidelines in the first and second phases.

VTE prophylaxis according to the guidelines			
phase	Received N (%)	Did not received N (%)	P-Value
I			
*before pharmacist intervention	171(85.1%)	30(14.9%)	0/11
II			
*after pharmacist intervention	96(91.4%)	9(8.6%)	

3.3. Discussion

Thromboembolic problems are one of the most important concerns after orthopedic surgery. Although recent studies have shown that the rate of VTE has decreased significantly (0-20%) [15], it is still an important and worrying problem.

Oster et al. reviewed data from US databases and found that in general, 2.2% of patients undergoing major orthopedic surgery develop thromboembolism within the first 90 days after hospitalization. They stated that 60% of these cases developed this problem after discharge from the hospital [16]. Thus, the use of an appropriate thromboprophylaxis method seems very necessary. Despite the numerous drugs that have been introduced for this purpose, there is still disagreement in choosing the appropriate drug with higher efficacy and fewer side effects [17-22].

LMWH, also known as enoxaparin, is a well-known and widely used drug that has been proven in several studies to be effective and safe [17, 19, 20]. It is prescribed in many medical centers after orthopedic surgery. In addition to prescribing or not prescribing thromboprophylaxis, VTE prevention is a major challenge in developing countries. In fact, not only is accurate prevention of VTE crucial, but it is also important to avoid incorrect anticoagulant therapy given the risk of bleeding [8]. According to the 2008 ACCP report on VTE prevention, only 78.8% of all patients in need of prophylaxis in the Middle East receive medication. Also, 66% of patients who are contraindicated for thromboprophylaxis and 78% of people who do not need thromboprophylaxis at all receive inadequate prevention [23].

Considering that most cases of VTE can be prevented through proper administration of anticoagulants, it seems necessary to individually assess the risk of thrombosis in patients admitted to the orthopedic ward and to consider appropriate anticoagulant drugs as prevention method. In a study conducted in Iran in 2019, Amirsadri et al. found that the use of enoxaparin to prevent thrombosis compared to heparin is not a cost-effective intervention [24].

The difference between this study and most of the existing studies on the effectiveness of specific anticoagulants administered in a particular type of surgery is that this study examines and modifies the thrombosis prevention process for patients admitted to the orthopedic ward and the degree of compliance with the guidelines available in this area.

In the first phase of the present study which was performed on 201 patients undergoing orthopedic

surgery in a hospital, based on the risk of thrombosis and assessment of the patient's condition and mobility, 161 (80.1%) patients were found to need prophylaxis, of which 143 (82.88%) received medication. Enoxaparin was prescribed to all 143 patients, three of whom (2.09%) were prohibited from taking enoxaparin due to their high creatinine levels. Therefore, the appropriate medication was not prescribed for them.

In the second phase, 105 orthopedic candidates were randomly admitted to the study. Four (6.15%) out of 65 patients who needed prophylaxis did not receive the drug despite pharmacist intervention. The reasons for not prescribing drugs to those patients were the lack of high risk and young age in 3 (75%) cases and the doctor's unwillingness to cooperate in 1 (25%).

The lack of direct use of scoring systems to determine the risk of thrombosis in the hospital has led to patients undergoing thromboprophylaxis based on the physician's discretion and the type of surgery performed. As a result, whether or not the doctor prescribes the drug, considering the risk of thrombosis for the patient, is ambiguous. Therefore, having a special risk assessment table for patients in their files seems necessary and efficient.

According to the results, 5 (12.5%) out of 40 patients who did not need prophylaxis received inappropriate medication because of a lack of proper risk assessment by the treating physician and a lack of pharmacist intervention. Moreover, 50 (76.92%) of 65 patients who needed prophylaxis received enoxaparin, despite heparin being recommended by pharmacist intervention. Reasons for the opposition to heparin administration in the present study were the unwillingness of the physician to cooperate in 32 (64%) cases and short hospital stay as well as the unwillingness to change medication in 18 (36%) cases.

Another reason for the doctors' rejection of heparin was the high workload in the orthopedic department due to heavy patient loads. In the physicians' opinion, because enoxaparin is injected only once a day, compared to heparin which is injected 2 to 3 times daily, use of enoxaparin reduced the workload in the department. A misconception about the administration of enoxaparin is that it is first on the drug list because of the alphabetical order of references. This arrangement, however, is not a reason to prioritize medication. Many doctors also believe that when the patient is in the ward for a short time and is scheduled to be discharged soon, changing the prescribed medication is not right for that patient.

It seems that the presence of resident pharmacists for continuous control of drug administration from the first day of hospitalization is necessary to solve the problem

of inappropriate thromboprophylaxis. It is also possible to increase the desire to perform such interventions by holding coordination meetings with relevant physicians and by preparing and implementing appropriate medication prescribing protocols, so that even in the absence of a pharmacist, any change in medication prescribing can be done automatically.

In total, out of 105 patients included in the current study, 65 (61.9%) needed prophylaxis and 10 (9.52%) received heparin with the intervention of a pharmacist. Doctors agreed to prescribe heparin in these patients because of high patient creatinine levels and the prohibition of enoxaparin use in 3 (30%) cases and physician justification by the pharmacist that heparin was effective in 7 (70%) cases.

Overall in the present study, 1 patient (2.74%) received heparin before the pharmacist intervention, but 10 (15.15%) patients received heparin after pharmacist intervention. Thus, pharmacist intervention increased heparin consumption by 12.41% and decreased enoxaparin consumption by 12.41%.

In phase I of this study, 171 (85.1%) out of 201 patients and in phase II 96 (91.4%) out of 105 patients were prescribed prophylaxis according to the guidelines. The results of this study showed that despite the intervention of a pharmacist to modify the process of thromboprophylaxis, no significant change was achieved in modifying the process of rational administration of drugs.

4. Conclusion

The limitations of this study include the lack of cooperation of physicians with pharmacists, diagnosis of the need for thromboprophylaxis of patients without the use of a scoring system, early discharge of patients, and incomplete patient records. It is believed that in the future, the implementation of training programs for physicians, the addition of a thrombosis risk card in the files of patients undergoing orthopedic surgery, and the necessary research to evaluate the effectiveness and side effects of various drugs in the prevention of thrombosis, can be a significant help in solving the problems of the medical and pharmaceutical community.

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Conflict of interest

The authors declare no conflict of interest.

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Ethics

Ethics committee approvals were obtained before the initiation of the study with the approval number of IR.SBMU.PHARMACY.REC.1398.042.

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