Journal of Molecular Biomarkers & Diagnosis
ISSN: 2155-9929

Chung et al., J Mol Biomark Diagn 2017, 8:3
DOI: 10.4172/2155-9929.1000329

Research Article OMICS International

Drug Utilization Evaluation (DUE) on Enoxaparin in Venous Thromboembolism (VTE) Prophylaxis for Hip and Knee Replacement Surgery

Yue Ling Chung[1]*, Kai Xin Ng[1], and Kah Weng Lai[2]

[1]*Department of Pharmacy, National University Hospital, Singapore*
[2]*Department of Orthopedics, National University Hospital, Singapore*

Abstract

Aim: The study aims to assess the adequacy and appropriateness of the use of chemical prophylaxis/enoxaparin in total knee and/or hip replacement (TKR and THR) surgery patients at National University Hospital (NUH) with respect to the compliance/non-compliance to NUH Venous-Thromboembolism (VTE) Prophylaxis Guidelines. This is done with the objective to identify potential gaps in current prescribing patterns that may require interventions to improve clinical efficacy and safety outcomes.

Methodology: A retrospective drug utilization evaluation was performed for NUH patients aged≥18 years old who have undergone TKR and/or THR surgery from 1st January to 31st May 2013 and excluded foreigners not residing in Singapore. The study indicators included compliance of chemoprophylaxis/enoxaparin prescribing patterns to NUH guidelines. Efficacy and safety related clinical outcomes in terms of VTE and hemorrhagic events respectively in a 3-months follow-up period post-surgery were also measured.

Results: A total of 127 patients were available for evaluation but data for 82 patients were collected and analyzed. Chemoprophylaxis prescribing patterns for only 46 (56.1%) patients were compliant to NUH guidelines in terms of indication. The need for chemoprophylaxis exceeded bleeding risks for 55 (67.1%) patients but only 30 (36.6%) patients were given chemoprophylaxis (enoxaparin). When enoxaparin was prescribed, none of the dosing regimens were compliant to NUH guidelines in all aspects of dose and frequency, prophylaxis duration and time of first dose initiation. During the 3-months follow-up, no bleeding events due to enoxaparin occurred. 9 (11.0%) patients developed thrombosis, 2 of which considered as clinically significant by physicians.

Conclusion: The study revealed the baseline chemoprophylaxis and enoxaparin usage patterns in NUH TKR and THR patients. The adverse clinical outcomes that occurred identified potential safety gaps within the prescribing practices, for which recommendations were made to improve the safe and effective use of VTE chemoprophylaxis in NUH post-surgical orthopedic patients.

Introduction

Venous thromboembolism (VTE), which includes deep vein thrombosis (DVT) and pulmonary embolism (PE), is well-recognized to contribute to significant mortality and morbidity in terms of chronic venous ulcers and post-phlebitis syndrome [1]. In several retrospective studies, the risk of fatal PE in patients with DVT is reported to be 5% and in patients with PE, 8% to 23% [2-4]. One of the major risk factors of VTE is orthopedic surgeries, where vascular injury during the surgery and immobilization pre/post-surgery considerably increases the chance of developing VTE [5,6]. However, the incidence of VTE may be reduced with the use of anti-thrombotic agents. In particular, the American College Chest Physician (ACCP) 2012 guidelines (9th Edition) have suggested the use of low molecular weight heparin (LMWH) over other recommended prophylactic agents in total knee replacement (TKR) and total hip replacement (THR) surgeries [7].

According to the findings of a meta-analysis presented in the ACCP 2012 guidelines, the use of LMWH consistently reduces asymptomatic DVT by 50% in TKR and THR surgery patients.[7] It was also previously reported that without thromboprophylaxis, the incidence of objectively confirmed DVT within 7-14 days following such major orthopedic surgeries was estimated to be 40% to 60% [8,9]. Coupled to the rising incidence of DVT in Asian populations, [1] the need to optimise VTE prophylaxis in post-surgical orthopedic patients has become increasingly important. Enoxaparin, an anti-Xa inhibitor, is one of the most commonly used LMWH for VTE prophylaxis in patients undergoing TKR and THR surgeries. However, there is currently a lack of consensus among various guidelines with regards to the prophylaxis dosing regimen of enoxaparin in TKR and THR surgery patients. The differences are summarized in Table 1.

National University Hospital (NUH) of Singapore has their own set of VTE Prophylaxis Guidelines for post-surgical orthopedics patients which recommendations were decided by the orthopedics department. This set of guidelines lists out the criteria for chemoprophylaxis, bleeding risks factors and recommendations for pharmacological prophylaxis when required. The NUH VTE Prophylaxis Guidelines can be found in Appendix 1.

Although there are guidelines that recommend the appropriate enoxaparin prophylaxis dosing regimen and identify at risked orthopedic surgery patients who should receive chemical thromboprophylaxis, there is still sub-optimal use of enoxaparin for VTE thromboprophylaxis in this group of patients. In a retrospective

***Corresponding author:** Yue Ling Chung, Department of Pharmacy, National University Hospital, Singapore, Tel: +65 6779 5555; E-mail: yue_ling_chung@nuhs.edu.sg

Received December 23, 2016; **Accepted** January 30, 2017; **Published** February 02, 2017

Citation: Chung YL, Ng KX, Lai KW (2017) Drug Utilization Evaluation (DUE) on Enoxaparin in Venous Thromboembolism (VTE) Prophylaxis for Hip and Knee Replacement Surgery. J Mol Biomark Diagn 8: 329. doi: 10.4172/2155-9929.1000329

Guidelines/References	Enoxaparin Dosing Regimen for VTE Prophylaxis in THR and TKR Surgery Patients			
	Dose	Frequency	Time of Initiation of First Dose	Duration
Manufacturer's Recommendations [10]	40 mg	OD	12 hrs pre-operatively	7-10 days or until risk of DVT diminishes
NUH in-house guidelines by orthopedics department [11]	As per manufacturer's recommendations			
ACCP 9th Edition [7]	40 mg	OD	≥12 hrs preoperatively or postoperatively	At least 10-14 days
Guidelines for Practice in Australia and New Zealand (4th edn) [12]	40 mg	OD	Not mentioned	5-10 days, except 28-35 days in THR surgery
National Institute for Health and Care Excellence (NICE) Guidelines 92 (Jan 2010) [13]	40 mg	OD	6-12 hrs after surgery	10-14 days for TKR surgery, 28-35 days in THR surgery
Drug Information Handbook 21st Edition[14-17]	30mg 40 mg (for THR only)	BD OD (for THR surgery only)	12-24 hrs after surgery 9-15 hrs before surgery	10 days or until risk of DVT diminishes 10 days (up to 35 days postoperatively) or until risk of DVT diminishes

Table 1: Differences in Enoxaparin prophylaxis dosing regimen recommended by various guidelines/references.

study that evaluated the appropriateness of enoxaparin use, it was reported that 40% of the 463 study participants from Lebanese hospitals received improper enoxaparin dosing [10-15]. This was mostly observed in the VTE prophylaxis group.

To the best of our knowledge, there are currently no known studies evaluating the use of enoxaparin in THR and TKR surgery patients in NUH and/or Singapore. A drug use evaluation (DUE) that systematically assesses current prescribing patterns would be useful in alerting local physicians on whether the use of enoxaparin for VTE prophylaxis in this group of patients has been appropriate and if any changes are required to ensure optimization of patient outcome in terms of postoperative patient morbidity and mortality. As such, the aims of this DUE are to

1) Evaluate the adequacy of VTE prophylaxis with enoxaparin or other chemo-thromboprophylaxis in THR and TKR patients.

2) Assess the appropriateness of use of enoxaparin, including the dose, frequency, indication, contraindications, duration of drug administration and time of first dose initiation.

3) Evaluate efficacy and safety related outcomes, in terms of VTE events and hemorrhagic events respectively, in a 3 months-follow up period [16], due to compliance or non-compliance with the NUH guidelines.

Methodology

Subject recruitment

All patients greater or equal to 18 years old who had undergone TKR and/or THR surgery at NUH from 1st January 2013 to 31st May 2013 were included in the study. This list of patients was obtained from an orthopedic surgeon at NUH. The cohort was subsequently checked to exclude patients who would mostly likely be lost to follow up, such as patients who were foreigners not residing in Singapore. A retrospective review of the medical records of the remaining patients was subsequently conducted.

Data collection

Pertinent information relevant to the demographics and other patient-related data, laboratory monitoring parameters, enoxaparin prescribing patterns, as well as efficacy and safety related outcomes, were gathered using the CPSS, Computerised Patient Records System (CPRS) and eIMR systems of NUH. Reference to case notes and scanned records were also carried out where applicable and possible. In order to ensure the completeness and consistency of the data collected, a pre-determined data collection form was designed and vetted by two senior pharmacists. All data extraction and collection was conducted by a pre-registration pharmacist. When there was any ambiguity in the process of data analysis and interpretation, a senior pharmacist was consulted to come to a consensus.

Demographics and other patient-related data including age, gender, race (Chinese, Malay, Indian or others), weight, height, drug allergies, surgery type and concurrent epidural and/or interactive medications such as anti-platelet agents, anti-coagulants, warfarin and non-steriodal anti-inflammatory drugs (NSAIDS) were collected. Additionally, data regarding patients' fit for chemoprophylaxis criteria (Criteria A: presence of thrombophilia and diseases associated with hypercoagulable states, Criteria B: previous history of VTE and/or Criteria C: 3 or more VTE risk factors) and presence of bleeding risks factors, as in accordance with the NUH VTE Prophylaxis guidelines, were gathered. Data on relevant laboratory monitoring parameters that was collected included hemoglobin (Hgb), hematocrit (Hct), platelet, serum creatinine, urea, AST, ALT, total bilirubin, INR, aPTT, PT and plasma anti-Xa activity. The renal function of each patient subject was calculated and estimated using the Cockcroft–Gault equation. It was also noted if patients were given mechanical prophylaxis or some form of anti-thrombotic agents for chemoprophylaxis.

For patients who were prescribed with enoxaparin for VTE prophylaxis, further data collection was conducted. This included information on the surgery details (date, time and duration) and prescribing patterns of enoxaparin (the dose, frequency, time of initiation of first dose of enoxaparin and duration of drug administration).

Finally, data on efficacy outcomes in terms of VTE events and safety outcomes with regards to hemorrhagic episodes in a 3 months follow-up period from the day of the surgery was recorded. This included information on whether there were any readmissions to the hospital after their discharge post-surgery.

The pre-determined data collection form that was used can be found in Appendix 2.

Study Indicators

This drug utilization evaluation involved an assessment of the process and outcomes of chemoprophylaxis/ enoxaparin usage due to compliance or non-compliance to NUH VTE prophylaxis guidelines. The process indicators were indication (whether patients were given chemoprophylaxis when appropriately indicated) and dosing regimen of enoxaparin when prescribed for VTE prophylaxis (regardless of the compliance to NUH guidelines with respect to the indications). The outcome indicators were efficacy related outcomes (in terms of VTE episodes) and safety related outcomes (in terms of documented

Group	Characteristics	On prophylaxis	Not on prophylaxis	Total
A	Fits Criteria for Prophylaxis and No Bleeding Risk	27 (32.9%)	25 (30.5%)	52 (63.4%)
B	Do not fit Criteria for Prophylaxis and No Bleeding Risk	11 (13.4%)	15 (18.3%)	26 (31.7%)
C	Fit Criteria for Prophylaxis and had Bleeding Risks	3 (3.7%)	1 (1.2%)	4 (4.9%)

Table 2: Results for compliance of chemoprophylaxis prescribing decisions to NUH VTE Prophylaxis guidelines.

hemorrhage events due to enoxaparin in CPSS2) in 3 months follow up period post-surgery.

Assessment criteria

The use of chemoprophylaxis was deemed to be appropriate if there is:

1. Absence of contraindications. This includes:

a. Adverse Reaction to Unfractionated Heparin (UFH) and LMWH.

b. History of Heparin Induced Thrombocytopenia (HIT).

2. Fit the Criteria for Chemoprophylaxis as in accordance with the NUH VTE prophylaxis guidelines and

a. With no bleeding risks or

b. With bleeding risks but the need for chemoprophylaxis exceed the bleeding risks.

Both the above criteria need to be fulfilled to be considered as an appropriate indication for chemoprophylaxis.

Enoxaparin usage was deemed to be appropriate if patients were prescribed with 40 mg once daily (OD) and 12 hours pre-operatively for 7-10 days, as in accordance with the NUH VTE prophylaxis guidelines.

Results

A total of 140 patients were identified to have undergone TKR and/or THR surgery from 1st January to 31st May 2013. All these patients were 18 years old and above. 13 patients were excluded from the study as they were foreigners not residing in Singapore and hence, a 3 months follow up period for their clinical outcomes in terms of efficacy and safety was not feasible. This leaves a remaining pool of 127 patients. However, data was collected and analysed for only 82 patients due to time constraints. From this final cohort of 82 patients, 65 (79.3%) were female. 75 (91.5%) of the patients had TKR surgery and 7 (8.5%) had THR surgery. The mean age was 65.1 years ± 8.57 years (range: 44-83 years). The majority, 34 (41.5%), of the patients were in the age range of 61-70 years. 52 (63.4%) of the patients were Chinese, 14 (17.1%) were Malay, 12 (14.6%) were Indians and the remaining 4 patients were of other races.

All 82 patients did not have any contraindications to the use of enoxaparin. In all cases where chemoprophylaxis was prescribed, only enoxaparin was used. For all patients not prescribed with any chemoprophylaxis, mechanical prophylaxis (i.e., calf pumps or TED stocking) were given in the absence of contraindications.

Part I: Assessment of compliance to NUH VTE prophylaxis guidelines in terms of indication

Within the cohort of 82 patients, chemoprophylaxis prescribing patterns for only 46 (56.1%) patients were compliant to NUH VTE guidelines in terms of indication, i.e., patients were prescribed with enoxaparin when appropriately indicated or were not given any chemoprophylaxis when not indicated.

55 (67.1%) patients fit the criteria for chemoprophylaxis and should be on chemoprophylaxis given that need for prophylaxis exceeded the bleeding risk. Interestingly, hyperlipidemia was the sole criteria for chemoprophylaxis for 45 of these patients. However, only 30 (36.6%) out of the 55 patients were given enoxaparin. To facilitate discussion, the cohort of 82 patients was categorized and analyzed as accordingly to Table 2.

(Group A) The fit criteria for chemoprophylaxis and no bleeding risk: 52 (63.4%) patients fell under this group and thus should have on some form of chemoprophylaxis as in accordance with the NUH VTE prophylaxis guidelines. However, only 27 (32.9%) patients in this group were prescribed with enoxaparin. The other 25 (30.5%) patients were not on prophylaxis, and hence, were not compliant to the guidelines in terms of indication.

(Group B) The did not fit criteria for chemoprophylaxis and no bleeding risk: 26 (31.7%) patients fell under this group and no chemoprophylaxis was necessary as in accordance with the NUH VTE prophylaxis guidelines. However, while 15 (18.3%) of the patients were not on prophylaxis, 11 (13.4%) were still given enoxaparin.

(Group C) The fit criteria for chemoprophylaxis and had bleeding risk: 4 (4.9%) patients were categorized under this group. 2 patients had a history of thalassemia, 1 had traumatic subdural hematoma (but was deemed stable enough by the doctors to start anti-coagulation) and the remaining 1 patient had active gastrointestinal bleeding. The former 3 patients were prescribed with enoxaparin while the latter patient was not given any form of chemoprophylaxis. Consultation with 2 senior pharmacists led to the consensus that the prescribing decisions for these 4 patients were compliant to the NUH guidelines; enoxaparin was only given in cases where the need for chemoprophylaxis was assessed to have exceeded the bleeding risks.

Part II: Assessment of compliance to NUH VTE prophylaxis guidelines in terms of enoxaparin dosing regimen

A total of 41 patients were given enoxaparin. The prescribing patterns of enoxaparin in these 41 patients were evaluated regardless of their compliance to NUH guidelines with respect to indication. The prescribing patterns were evaluated in terms of the:

1. Dose and frequency.

2. Duration of prophylaxis and

3. Time of first dose initiation.

None of the prescribing patterns of enoxaparin in the 41 patients complied to the NUH guidelines in all of the above 3 aspects.

All the patients prescribed with enoxaparin had a creatinine clearance of greater than 30mL/min and thus no dose adjustment was required.

Dose and frequency of enoxaparin administration: Whenever there was a dose change during the study period, the dosing which was most frequently prescribed for the patient was selected.

Among the 41 patients prescribed with enoxaparin, only 25 (61.0%) patients were prescribed 40 mg OD and thus complied with the NUH guidelines which follow the manufacturer's recommendations. For the

remaining 16 patients, 9 (22.0%) were prescribed 30 mg OD, 4 (9.8%) were prescribed 60 mg OD, 2 (4.9%) patients were prescribed 20 mg OD and 1 (2.4%) was prescribed 50 mg OD.

Duration of prophylaxis: None of the patients had a prescribed duration of enoxaparin administration that followed the NUH guidelines' recommendations of 7-10 days. Most, 31 (81.6%), of the patients were prescribed with enoxaparin for 1-3 days, 6 (15.8%) were prescribed for 4-6 days and 1 (2.6%) was prescribed for greater than 10 days. 3 patients on enoxaparin were omitted from analysis for duration prophylaxis. Of these 3 patients, 2 developed thrombosis and were treated while the other patient developed chest pain. For the latter patient, impression was non-ST segment elevated myocardial infarction (NSTEMI) precipitated by post-operation anemia and anti-coagulants were held off.

Time of initiation of first dose of Enoxaparin: For the purpose of evaluating the time of first dose initiation in this study, a deviation of 2 hours from the recommended 12 hours was allowed.

None of the patients were initiated on enoxaparin 12 ± 2 hours pre-operatively as recommended by the NUH guidelines. Most of the patients were initiated on enoxaparin post-operation; 21 (52.2%) were started 15-24 hours post-surgery, 10 (24.4%) were started greater than 24 hours post-surgery and 6 (14.6%) were started less than 10 hours post-surgery. The rest of the patients were started on enoxaparin pre-operation; 2 (4.9%) were started 15-24 hours pre-surgery and 2 (4.9%) were started greater than 24 hours pre-surgery.

Part III: Evaluation of outcomes with respect to compliance/non-compliance to nuh vte prophylaxis guidelines in a 3-month follow up post-surgery

Safety related outcomes: Hemorrhagic events: There were no events of hemorrhage due to enoxaparin according to documentations in CPSS2. The case notes were not referred for this aspect due to time constraints.

Efficacy related outcomes: VTE episodes: A total of 9 (11.0%) patients developed thrombosis. All events of thrombosis were confirmed by Doppler Ultrasound scan (US) or CT angiogram.

No events of thrombosis occurred when NUH guidelines with respect to indication were complied. Among the 9 patients who developed thrombosis, non-compliance to NUH guidelines with respect to chemoprophylaxis indication was found in 5 patients, of which 2 thrombosis events were considered as clinically significant by the physicians. Non-compliance to NUH guidelines with regards to enoxaparin dosing regimen was found in the remaining 4 events of thrombosis that occurred.

Thrombosis in pulmonary arteries/proximal veins: One patient developed pulmonary embolism in the pulmonary arteries, confirmed by CT angiogram on post-operation day (POD) 4 and was treated with anti-coagulants. This was a 78 years old male patient who weighed 69.1 kg with a BMI of 24.5 kg/m^2. Having a medical history of hyperlipidemia, she fitted criteria A for chemoprophylaxis according to the NUH VTE prophylaxis guidelines. It was also noted that she had limited mobility of less than 10 meters that required moderate supervision by the physiotherapist. However, no chemoprophylaxis was prescribed for this patient and thus compliance to NUH VTE prophylaxis guidelines in terms of indication was absent.

Another patient developed partial thrombosis on the left superficial femoral vein, confirmed by Doppler US on POD3, and was treated with anti-coagulants. This patient was a 61 years old female who weighs 41 kg with a BMI of 20.1 kg/m^2. She did not actually fit the criteria for chemoprophylaxis according to the NUH guidelines and thus chemoprophylaxs was not indicated. However, she was still prescribed with enoxaparin but at a subtherapeutic dose of 30 mg OD, initiated 29 hours post-operation.

Thrombosis in distal veins: One patient developed complete thrombosis in the muscular branch vein at the medial calf, as confirmed by the Doppler US on POD3, and was treated. Although prescribed with enoxaparin when appropriately indicated, enoxaparin was initiated 22 hours post-operation.

Six other patients developed thrombosis in the tibial, peroneal and/or popliteal veins. There was non-compliance to NUH guidelines in terms of indication in 3 of the cases; these 3 patients fit the criteria for chemoprophylaxis and had no bleeding risks according to the guidelines but were not prescribed with chemoprophylaxis. However, 1 of these patients experienced a downward trending of hemoglobin level (Hgb=8.2 (POD1)→ 7.7 (POD2)) that required blood transfusion. This could have led to the decision to hold off enoxaparin administration. Non-compliance to NUH guidelines in terms of dosing regimen was found for the other 3 cases. 2 of these patients were prescribed sub-therapeutic doses of 30 mg OD. While none of them were initiated with enoxaparin at the recommended time of 12 ± 2 hours pre-operation, 1 patient had a delayed initiation of enoxaparin (40 mg OD) 28 hours post-operation. However, none of these six cases of thrombosis were considered clinically significant by the physicians and thus were not treated.

Discussion

From the present DUE, it was found that the compliance rates to NUH VTE Prophylaxis guidelines for post-surgical TKR and THR patients in terms of all 3 aspects of indication, dose and frequency, duration of prophylaxis and time of initiation of first dose of enoxaparin were not 100%.

When NUH VTE prophylaxis guidelines in terms of indications were complied, no events of hemorrhage and thrombosis occurred. However, the observed safety outcomes in terms of hemorrhagic events might have been confounded by some factors, such as the inappropriate enoxaparin dosing regimens that were non-compliant to the NUH guidelines. For example, although appropriately indicated patients were prescribed with enoxaparin, the sub-therapeutic short duration of prophylaxis of 1-3 days could have translated to lower bleeding risks and thus, accounting for the absence of bleeding episodes.

On the other hand, non-compliance to the NUH VTE prophylaxis guidelines in terms of indications was found in 5 of the thrombosis events that occurred, 2 of which were considered as clinically significant by the physicians. Between these 2 clinically significant thrombosis events, the patient who developed a thrombus in the femoral vein was considered as an outlier. For this patient, a thrombus developed despite being assessed as low risk for VTE and thus did not fit the criteria for chemoprophylaxis. Furthermore, the thrombus developed even when enoxaparin was prescribed for prophylaxis, although initiated late at a sub-therapeutic dose of 30 mg OD.

Among the 55 (67.1%) patients who were appropriately indicated for chemoprophylaxis, 25 (30.5%) patients were not given enoxaparin. However, the decision to hold off enoxaparin in 8 of these 22 patients may be justifiable in view of documented post-operation anaemia or low hemoglobin counts that required blood transfusion. Documented

post-operation anaemia and/or low hemoglobin counts that required blood transfusion were not considered as "bleeding risk factors" for the purpose of this study as they were not specified in the NUH VTE prophylaxis guidelines. This is a limitation of the study and probably of the guidelines as well. As mentioned earlier under section 4 part III, patients were considered as having an "active bleed" only if it was documented as such in the CPSS2 discharge summaries.

Enoxparin dosing regimens that deviated from the recommendation of 40 mg OD could have been explained by factors such as old age or extremities of patients' weight (e.g. 41 kg or 98 kg). However, adjusted weight-based prophylaxis enoxaparin dosing [17] is currently recommended for only morbidly obese patients with a BMI ≥ 40 kg/m^2, which none of the patients in this study cohort had.

Similar number of episodes of thrombosis occurred when there was non-compliance to NUH guidelines with respect to indication (5 episodes) and enoxaparin dosing regimen (4 episodes). However due to the limitations of a small sample size, it remains uncertain as to whether non-compliance to NUH guidelines with respect to indication held as equal importance as that to enoxaparin dosing regimen.

Although this DUE had a relatively small patient sample size, the study detected a total of 9 (11.0%) thrombosis events, 2 of which were clinically significant. To improve the safe and effective use of enoxaparin in post-surgical TKR and THR patients in NUH, recommendations that can be made include:

1. To review and revamp current guidelines, and make it available in the care path.

• For example, the term "active bleed" under the section of "Bleeding Risk Factors" in the guidelines could be better defined, such as in terms of the number of hemoglobin units decrease or amount of blood infused post-surgery. The conditions for "until risk of DVT diminishes" under the dosing guide section could also be better detailed, which may then justify the shorter duration of enoxapain use in DVT prophylaxis in real life clinical practice.

• To design a form based on the revamped guidelines that allow the doctors to check against the corresponding chemoprophylaxis criteria and determine the need for chemoprophylaxis.

2. Devise a system (for example a pop-up signal) that prompts the correct use of enoxaparin when the doctor uses once daily dosing.

3. Train and educate the doctors and pharmacists about the appropriate chemoprophylaxis indication and dosing regimen of enoxaparin when used for prophylaxis.

4. Share the findings of the study with the orthopedics department to raise awareness.

Conclusion

In conclusion, there is sub-optimal use of enoxaparin for VTE prophylaxis in patients who have undergone TKR and/or THR surgery and are at risk of VTE. This is in terms of indication, dose and frequency, duration of prophylaxis and time of first dose initiation of enoxaparin. The adverse clinical outcomes that occurred during the study period pointed to potential safety gaps within the prescribing practices, for which recommendations were made to improve the safe and effective use of chemoprophylaxis/enoxaparin in post-surgical orthopedic patients in NUH.

References

1. http://annals.edu.sg/cpd0302a.html
2. Anderson FA Jr, Wheeler HB, Goldberg RJ, Hosmer DW, Patwardhan NA, et al. (1991) A population-based perspective of the hospital incidence and case-fatality rates of deep vein thrombosis and pulmonary embolism: the Worcester DVT study. Arch Intern Med 151: 933-938.
3. Dalen JE, Alpert JS (1975) Natural history of pulmonary embolism. Prog Cardiovasc Dis 17: 259-270.
4. Alpert JS, Smith R, Carlson J, Ockene IS, Dexter L, et al. (1976) Mortality in patients treated for pulmonary embolism. JAMA 236: 1477-1480.
5. http://orthoinfo.aaos.org/topic.cfm?topic=A00219
6. Stamatakis JD, Kakkar VV, Sagar S, Lawrence D, Nairn D, et al. (1977) Femoral vein thrombosis and total hip replacement. Br Med J 2: 223-225.
7. Falck-Ytter Y, Francis CW, Johanson NA, Curley C, Dahl OE, et al. (2012) Prevention of VTE in orthopedic surgery patients: Antithrombotic Therapy and Prevention of Thrombosis, (9thedn): American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 141: e278S-325S.
8. Geerts WH, Bergqvist D, Pineo GF, Heit JA, Samama CM, et al. (2008) Prevention of venous thromboembolism: American college of chest physicians evidence-based clinical practice guidelines (8thedn). Chest 133: 381S-453.
9. Geerts WH, Pineo GF, Heit JA, Bergqvist D, Lassen MR, et al. (2004) Prevention of venous thromboembolism: the seventh ACCP conference on antithrombotic and thrombolytic therapy. Chest 126: 338S-400.
10. http://www.medicines.org.uk/emc/medicine/24345/SPC/Clexane+pre-filled+syringes
11. Venous Thromboembolism (VTE) Risk Stratification and prophylaxis guidelines. National University Hospital, Singapore. Hospital Administrative Policy; 2012. NUH-HAP-MAQ-055.
12. Fletcher J, MacLellan D, Baker R, Chong B, Fisher C, et al. (2012) Prevention of venous thromboembolism. The Australia and New Zealand Working Party on the Management and Prevention of Venous Thromboembolism, (4thedn), Australia, Newzealand.
13. Venous Thromboembolism: Reducing the risk (2010) National Institute for Health and Care Excellence (NICE) Guidelines 92.
14. Drug Information Handbook (21edn), 2012-2013. Enoxaparin, 636.
15. Zeitoun AA, Nassif JG, Zeineddine MM (2011)The appropriateness of enoxaparin use in Lebanese hospitals: a quality evaluation study. Int J Clin Pharm 33: 934-941.
16. White RH, Romano PS, Zhou H, Rodrigo J, Bargar W (1998) Incidence and time course of thromboembolic outcomes following total hip or knee arthroplasty. Arch Intern Med 158: 1525-1531.
17. http://www.uptodate.com.libproxy1.nus.edu.sg/contents/enoxaparin-drug-information?source=search_result&search=enoxaparin&selectedTitle=1~99#F165080