International Journal of Orthopaedics Sciences

ISSN: 2395-1958
IJOS 2019; 5(3): 650-654

www.orthopaper.com
Received: 02-05-2019
Accepted: 06-06-2019

Dr. M Rohith Reddy
Senior Resident, Department of Orthopedics, Sanjay Gandhi Institute of Trauma and Orthopedics, Bengaluru, Karnataka, India

Dr. Shaik Mohasin Kamal
Consultant, Department of Orthopedics, MJ Naidu Hospital, Vijayawada, Andhra Pradesh, India

Dr. H Bala Krishna Gadigar
Professor and Head, Department of Orthopedics, PES Institute of Medical Sciences & Research Centre, Kuppam, Andhra Pradesh, India

Dr. Prasad Soraganvi
Professor, Department of Orthopedics, PES Institute of Medical Sciences & Research Centre, Kuppam, Andhra Pradesh, India

Dr. RP Raghavendra Raju
Assistant Professor, Department of Orthopedics, PES Institute of Medical Sciences & Research Centre, Kuppam, Andhra Pradesh, India

Correspondence
Dr. Shaik Mohasin Kamal
Consultant, Department of Orthopedics, MJ Naidu Hospital, Vijayawada, Andhra Pradesh, India

Efficacy of enoxaparin as athromboprophylactic agent in major lower limb orthopaedic surgeries

Dr. M Rohith Reddy, Dr. Shaik Mohasin Kamal, Dr. H Bala Krishna Gadigar, Dr. Prasad Soraganvi and Dr. RP Raghavendra Raju

DOI: https://doi.org/10.22271/ortho.2019.v5.i3l.1607

Abstract
Venous Thromboembolism (VTE) which consists of Deep Vein Thrombosis (DVT) & Pulmonary Embolism (PE) is a potentially fatal & common complication following major lower limb orthopaedic surgeries like Hip, Knee Arthroplasty & Hip fracture surgeries which fall under highest risk category for VTE stratification. Analysis of selected Indian articles show that rates of DVT with prophylaxis is 8% and without prophylaxis 14%. Therefore VTE prophylaxis is essential to prevent the mortality and morbidity associated with it. Low Molecular weight heparins like Enoxaparin is one of the leading anticoagulants registered for use worldwide and has a long track record of over several years for safety and efficiency in orthopaedic surgeries. 180 patients undergoing Surgeries for fracture around Hip, Femur fracture surgery, patients undergoing Hip and Knee Arthroplasty were given prophylaxis for DVT in the form of Inj. Enoxaparin 40 Mg S/C once a day for 10 days starting 12 hours after epidural catheter removal. Three Bilateral lower limb venous Doppler scans were done in all the patients, one at the time of admission, one on eleventh post op day and another on thirtieth post-operative day to look for development or progression of deep vein thrombosis. Only One Patient (0.55%) showed ultrasonographic evidence of proximal asymptomatic Deep Vein Thrombosis on the eleventh post-operative day. Patient was treated for the same and the thrombus resolved while on treatment as shown by repeat Doppler scan done on twentieth day following detection. No cases of Fatal Pulmonary embolism or major complications were noted in the study. Enoxaparin is a safe and effective thromboprophylactic agent when used for the duration of 10 days post operatively in Major lower Limb orthopaedic Surgeries.

Keywords: Enoxaparin, athromboprophylactic agent, major lower limb orthopaedic surgeries

Introduction
Venous Thromboembolism (VTE) which consists of Deep Vein Thrombosis (DVT) & Pulmonary Embolism (PE) is a potentially fatal & common complication following major lower limb orthopedic surgeries like Hip, Knee Arthroplasty & Hip fracture surgeries which fall under highest risk category for VTE stratification [1]. The rates of complications such as deep vein thrombosis and pulmonary embolism have shown to be around 40-60% within 7-14 days following major lower limb orthopedic surgeries without prophylaxis. Most of these thrombi resolve spontaneously, however a small percentage (1-4%) will develop into symptomatic venous thrombo embolism. The incidence of fatal PE in Patients not receiving thromboprophylaxis ranges from 0.3-1% following Total Joint Arthroplasty (TJA) and around 3.6% after Hip fracture surgery (HFS) [2]. Analysis of selected Indian literature search shows the incidence among thromboprophylaxis receiving group was 8%, where as it was higher - 14% in patients not receiving any form of prophylaxis.[3].The most dreaded complication of VTE is Pulmonary Embolism. Long term complications like Post-Thrombotic Syndrome (PTS) are frequent & disabling. Fatal PE, the most dramatic event of VTE accounts for 10% of hospital deaths and is the most common preventable cause of sudden unexplained deaths. 75% of those who die, do so within one hour of onset of the symptoms [1].
Both DVT & PE can clinically be silent or Asymptomatic and difficult to diagnose & hence not suspected. Even if symptomatic, the clinical features are non-specific and requires objective conformation [4, 5].

Majority of thrombi start in deep veins of calf. Most of them regress spontaneously. But 30% of them extend proximally into deep veins of thigh, which if untreated are associated with 50% chance of PE or recurrent VTE or a 5-10% chance of fatal PE. Chronic Thrombotic Pulmonary Hypertension (CTPH), Post Thrombotic Syndrome, Chronic Venous Insufficiency due to untreated and unrecognized DVT is associated with considerable morbidity & reduces the quality of life [1].

Most Proximal DVT can resolve without clinical sequelae, but some 50% of them are more likely to result in pulmonary embolism than distal DVT. The highest risk of occurrence of DVT has been reported to be on the fourth Post-Operative day and the second highest on the thirteenth day. The highest incidence of fatal PE occurs in the second week after surgery. The risk is supposed to exist for three months after surgery [6].

The Virchow's triad of factors for thrombogenesis-Venous Stasis, Hypercoagulability & Endothelial Injury-are seen in major lower limb orthopedic surgeries. The positioning of limb during surgery, localized post-operative edema and limitations in mobility immediately after surgery, all play a role in venous stasis and the consequent reduction of blood flow. During surgery, manipulation of the limb, heat reaction resulting from the use of cement, and other aggressions can also activate thrombogenicity factors that will manifest trophism for areas of vascular lesion and stasis [7].

On the other hand, blood loss can reduce Anti-Thrombin 3 levels and inhibit the endogenous fibrinolytic system, enabling the formation and growth of thrombi at all levels. Thus Orthopedic Surgery is a potential stimulus for thrombogenesis [7].

VTE is preventable mortality & morbidity, VTE prophylaxis is cost effective. It reduces DVT by half & PE by two third. It saves lives. It is number one measure to ensure safety of hospitalized patients [4, 8].

The issue is all the more relevant today as the number of joint arthroplasties and trauma surgeries for lower limb fractures has seen a manifold increase in the last few years, with very few surgeons offering some form of prophylaxis. Also there are medico-legal implications of not subjecting the patient to some form of prophylaxis, as some consider this as an act of negligence [9].

Primary prophylaxis for VTE has been shown to be more cost effective than case finding or investigations and treatment [1].

DVT can be diagnosed by a number of diagnostic modalities. Doppler USG is non-invasive, cost effective, can be used repeatedly and matches with the sensitivity and specificity of venography as far as proximal DVT is concerned [3, 6].

Optimal VTE prophylaxis is with Low Molecular Weight Heparins (LMWH). Enoxaparin is one of the leading agents in this class of anti-coagulants, being registered for use worldwide, its superiority over mechanical prophylaxis and Unfractionated Heparin (UFH) has been proved in several studies. The risk of bleeding is small (2%) and acceptable considering the dramatic decrease in proximal thrombi which are at a high risk of embolization [3, 8].

Methodology

A prospective study including 180 patients undergoing surgery for Major Trauma-(Hip fracture surgeries, Intertrochanteric fracture, Fracture neck and Shaft femur) THA, Hemiarthroplasty, TKA was conducted at our institute. All patients gave informed consent. All patients undergoing the study were interviewed and comprehensive clinical history and examination was conducted on them to rule out presence of risk factors for thromboembolism such as history of smoking, alcohol consumption, chronic venous insufficiency, stroke, varicose veins, malignancy, renal insufficiency, recent myocardial infarction, heart failure, who were taking oral contraceptives, or on steroidal/hormonal/ anticoagulant drugs for any medical condition.

Preoperative assessment for DVT was done in all patients on both the lower limbs by color Doppler ultrasonography, using Samsung HS 70 A ultrasound machine using a linear array high frequency probe 10-12 MHz with grey scale and color Doppler mode.

Color Doppler assessment included bilateral common femoral vein, superficial femoral, popliteal, anterior tibial and posterior tibial veins.

They were assessed for flow, visualized thrombus, compressibility and augmentation.

A diagnosis of DVT was made when there as visualization of thrombus, absence of flow, lack of compressibility or lack of augmentation

Patients were evaluated every day for signs and symptoms of Deep Vein Thrombosis like pain in the lower limbs, fever, calf tenderness, swelling of the lower limbs, pain elicited in the calf on dorsiflexion of ankle (Homan's sign), Pain elicited on squeezing the calf muscles (Moses sign).

Intra operative observation

1. Type of Anesthesia
2. Type of Surgery
3. Duration of Surgery
4. Tourniquet Time

Post-operative examinations symptoms

1. Pain in the calf and thigh
2. Chest Pain
3. Breathlessness
4. Hemoptysis
5. Irritability
6. Fever

Sign's

1. Swelling
2. Pitting edema
3. Local Rise of temperature
4. Calf muscle tenderness (Moses sign)
5. Homan's Sign

Pharmacological prophylaxis

DRUG: Inj. Enoxaparin

DOSAGE: 40 Mg subcutaneous once a day-starting 12 Following epidural catheter removal post-surgery.

Duration of prophylaxis: 10 days.

Complication due to prophylaxis

1. Wound hematoma
2. Erythema
3. Prolonged wound drainage
4. Haemarthrosis.
5. Major bleeding.

Follow-up

Patients were monitored everyday clinically for signs and symptoms of DVT during patients hospital stay.

Bilateral lower limb Venous Doppler was done on 11th day at the time of discharge and 30th day following surgery (one month follow up).

Results

All patients in the study group were given VTE prophylaxis with Inj. Enoxaparin. Asymptomatic proximal DVT was seen post operatively in a 70 Year old Female patient (Case No 9) who had Chronic Asthma, Hypertension and Rheumatic Heart Disease. This patient had undergone CRIF with PFN fixation for Right Intertrochanteric Fracture femur. DVT was detected by color Doppler USG on the 11th post op day scan. She was treated for DVT and followed up with frequent repeat Doppler scans. Repeat Doppler scan done 20 days following detection showed resolution of thrombus while on treatment. None of the other patients had DVT or PE pre or post operatively as evaluated clinically or by Doppler scan.

Minor bleeding complications due to Inj. Enoxaparin prophylaxis was seen in three patients. Wound Hematoma was seen in one patient, wound bruising in another patient, wound bruising with fever in one patient. All the three patients were on Enoxaparin for VTE prophylaxis. All the patients were treated with Antibiotics and analgesics for 10 days. None of the patients had thrombocytopenia or major hemorrhage. No patient had distal DVT, symptomatic DVT or Pulmonary Embolism.

This study includes 180 patients who have undergone Surgeries for fracture around hip and femur fracture surgery, Arthroplasty- hip and knee of 108, 48 and 24 patients respectively. All patients were investigated with pre-operative Doppler scan, with blood investigation like PT and aPTT. All patients received Thrombo prophylaxis in form of Inj. Enoxaparin 40mg subcutaneous, once a day for 10 days post operatively starting 12 hours following epidural catheter removal. Post-operative follow up venous Doppler scan were done on 11th day and 1 month following surgery. It was noted that, proximal asymptomatic DVT was found in one patient who underwent surgery for Intertrochanteric fracture of femur. In the rest of 179 patients no evidence of DVT was found in any Doppler scans. Also no symptomatic or fatal pulmonary embolism were noted in any patients.

The Study showed 0.55% of asymptomatic proximal DVT detected during 11th post op day follow up scan. DVT resolved with treatment during follow up scans. The thrombus did not propagate proximally.

Total number of patients who underwent DVT prophylaxis were 180. Proximal asymptomatic DVT was found in one patient during second follow up Doppler scan. This is 0.55% of the total study of 180 patients. The DVT resolved with treatment as seen during follow up ultrasound scan.

Table 1: Percentage of DVT

Total No of cases	No DVT	With DVT
180	179	1
	99.44%	0.55%

Table 2: Complications of prophylaxis

	No of Patients	Complications Found		% of Complications
Total	180	Total complications	3	1.6%
Total No of Hip Arthroplasty	48	Wound Hematoma	1	0.55%
Total No of TKR	24	Local Bruising	1	0.55%
Total No of surgeries for fracture around hip and femur fracture surgery	108	Fever with local bruising	1	0.55%

Study included 180 patients who had the following as risk factors- 32 type 2 diabetes, 21 hypertensives, 10 with both diabetes and hypertension, 43 smokers, 5 with varicose veins, 145 were above 40 years of age, 2 were on OCP's, 156 patients had surgery lasting for more than 2 hours, 12 were immobilized for more than 72 hours following surgery.

Table 3: Risk factors

Risk factors		No. of patients
Diabetes Mellitus		32
Hypertension		21
Diabetes and Hypertension		10
Smoking		43
Varicose veins		5
H/O VTE		0
Age>40 Years		145
OCP's		2
Duration of surgery lasting for more than 2 hours than 2 hours		156
Duration Of Immobilisation > 72 Hrs		12
Others	RHD	1
	HIV	1

Discussion

VTE includes DVT and PE. It is the 3rd leading cause of death from cardiovascular causes after MI and Stroke. VTE represents a global problem, especially in Western population, where it has been studied and documented extensively. The most feared complication in lower limb orthopedic surgery has been DVT, which may result in lethal Pulmonary Embolus. The incidence of venographic DVT and Proximal DVT within 7-14 days of Major lower limb orthopedic surgeries in patients who have no Thromboprophylaxis has been 40%-60% and 10%-30%, respectively. The symptomatic VTE is around 3-7% in various studies. The use of Thromboprophylaxis has brought down the rate of fatal PE to 0.1% in 90 days after surgery [19].

Scarcity of Indian studies on VTE and Thromboprophylaxis compels us to use the data, which is based on Western population. Very few studies are available on Indian patients with VTE and using Thromboprophylaxis [10].

Velu Nair [11] *et al.* in their retrospective study of 795 patients undergoing major orthopedic surgery given short term prophylaxis with 7-11 days has shown an incidence of DVT to be 3.27% with prophylaxis.

NK Chandra *et al.* [12] in their comparative study of patients undergoing major lower limb orthopedic surgeries have shown an incidence of 2.8% with prophylaxis and it was 7.5% in those who did not receive thromboprophylaxis

R K Sen *et al.* [3] in his article discusses the incidence of DVT and the role of Thromboprophylaxis in Indian patients who have sustained major orthopedic trauma.

The Incidence of VTE among thromboprophylaxis-receiving group was 8%, where as it is much higher-14.49% in patients not receiving any form of prophylaxis [3].

In our study the incidence of DVT with prophylaxis with LMWH (Enoxaparin) was found to be 0.55%.

Patients undergoing MLLOS (Major Lower Limb Orthopedic Surgery)-Hip or KNEE Arthroplasty-or HFS (Hip Fracture Surgery) are in the highest category for VTE solely on the

basis of orthopedic procedure itself. The rates of VTE events in the absence of prophylaxis are as follows- Calf DVT-40% to 80%, Proximal DVT 10% to 20%, Clinical PE 4% to 10%, Fatal PE 0.2% to 5%. Hip Replacement poses greater risk than Knee Replacement. Although the risk of proximal DVT is most concerning, patients may develop post-Phlebitic syndrome and a prior VTE, even if distal, increases the risk for subsequent events. Another important factor is that there is no way to predict which patients will develop symptomatic DVT [13].

Jose Bosque *et al*. [14] states that majority of DVT may be asymptomatic but can lead to later long term morbidity with symptomatic events. Untreated and unrecognized DVT can lead to recurrent thromboembolism, Pulmonary Embolism, Post-Phlebitic syndrome, CTPH (Chronic Thrombotic Pulmonary Hypertension), all of which can result in reduced quality of life and increased health care costs.

Jawed fared *et al*. [15] in their study concluded that LMWHs have replaced UFH as the gold standard anti-thrombotic agent. Enoxaparin is the LMWH that is commonly used for both VTE prophylaxis and treatment. Enoxaparin has the largest body of clinical evidence supporting its use across the spectrum of VTE management and has been used as the reference standard comparator anticoagulant in trials of new anti-coagulants

Bharathi Kalyani *et al*. [16] conducted a systematic review of literature using Medline database and showed that Enoxaparin was found to be more cost effective in orthopedic surgeries. Enoxaparin has shown greater safety and efficacy in VTE prophylaxis. In a study by Jan Won Mong *et al.* Enoxaparin has proved to be safe and efficacious in VTE prophylaxis. In our study Enoxaparin was used as the thromboprophylactic agent.

Thromboprophylaxis in necessary and it should be continued for approximately 7 to 9 days.

Clinical Practice guidelines for VTE prophylaxis have been established by several professional bodies, but two important ones are those of American College of Chest Physician guidelines (ACCP) and American Academy of Orthopedic Surgeons (AAOS).

In 2011 & 2012, respectively, the AAOS & ACCP published their recent guidelines on VTE prophylaxis after THA &TKA. These recommendations show greater concordance & both recognize the delicate balance between efficacy & safety. Both recognize that presence of an asymptomatic DVT may be of little or no consequence to the patient and additional focus was placed on bleeding & wound drainage.[17]

Clinical Practice guidelines for VTE prophylaxis have been established by several professional bodies, but two important ones are those of American College of Chest Physician guidelines (ACCP) and American Academy of Orthopedic Surgeons (AAOS).

In 2011 & 2012, respectively, the AAOS & ACCP published their recent guidelines on VTE prophylaxis after THA &TKA. These recommendations show greater concordance & both recognize the delicate balance between efficacy & safety. Both recognize that presence of an asymptomatic DVT may be of little or no consequence to the patient and additional focus was placed on bleeding & wound drainage [17].

Yngve Falck Ytter *et al*. [8] in his article in CHEST supplement 2012 on VTE prophylaxis states that the risk of VTE is especially significant for patients undergoing Orthopedic Surgery for traumatic injuries with a Fatal PE of 2.5%-7.5%. The risk of VTE is highest close to surgery and the mean time of diagnosis for thromboembolic events is 7 days after TKA and 17 days after THA with a combined 35 day untreated base-line risk for symptomatic VTE of 4.3% VTE. Prophylaxis reduces the risk by 40-50% and PE by two-thirds [8].

In our study of 180 patients undergoing major lower limb orthopedic surgeries (surgeries for fracture around hip, femur fracture surgery, Hip and Knee arthroplasty) only one patient (0.55%) developed DVT with prophylaxis on eleventh post-operative day. Patient was asymptomatic. This patient was treated for the same and repeat venous Doppler scan done twenty days following detection showed resolution of the thrombus while on treatment.

Velu Nair *et al*. [11] in their study of 795 patients with VTE prophylaxis with Enoxaparin in orthopedic surgeries has shown a minor bleeding complication rate of 5.78%, while in our study minor complications of VTE prophylaxis were seen in three cases (1.6%).

Among them wound hematoma in one case, local bruising in one, Fever with local bruising in another. No patient had pulmonary Embolism; no major bleeding complications were noted

The duration of prophylaxis for 10 days, as given in our study has shown to be safe and effective for VTE prophylaxis.

Conclusion

- With our study we conclude that LMWH - Enoxaparin is a cost effective thromboprophylactic agent when used for the duration of 10 days post operatively in Major lower Limb orthopedic Surgeries.
- Symptomatic and Asymptomatic venous thromboembolism can exist in patients with major lower extremity fractures and replacements.
- Associated medical co morbidities may accentuate the same.
- Thromboprophylaxis is an essential lifesaving intervention and reduces mortality and morbidity.

References

1. R Parekh, SK Todi *et al*. Consensus development recommendations for role of LMWH in prophylaxis of VTE: An Indian perspective. Suppliment of JAPI Jan 2007; 55.
2. Gandhi Nathan Solayar *et al*. Thromboprophylaxis and Orthopedic Surgery: Options and Current Guidelines. Malays J Med sci. 2014; 21(3):71-77.
3. Ramesh K Sen *et al*. Is routine thromboprophylaxis justified amoung Indian patients sustaining major orthopedic trauma- A systematic review. Indian journal of Orthopedics. 2011; 45(3):197-207.
4. VK Kapoor. Venous Thromboembolism in India. The Medical Journal of India. 2010; 23(4).
5. Pantep Angchaisuksiri. VTE in Asia-An unrecognized and untreated problem. Thrombosis and hemostasis, 2011, 106(4).
6. V Jain, B Dhaon, Jaiswal *et al*. Postgrad Med J Deep vein thrombosis after THA and TKA in Indian patients. 2004; 80(950):729-731.
7. LEG Leme *et al*. Prophylaxis of venous thromboembolism. Rev Bras Ortop. 2012; 47(6):685-93.
8. Falck Ytter *et al*. Prevention of VTE in orthopedic surgery: Chest. 2012; 141(2):278-325.
9. AP Mavalankar. Routine Chemoprophylaxis for DVT in Indian patients: Is it justified? IJO. 2007; 41:188-193.
10. Sudhir Kumar. VTE inMajor lowerlimb Orthopedic

Surgery. Indian Journal of Orthopedics, 2013, 47.
11. Velu Nair, Ratheesh *et al*. A Comparative study of extended versus short term thromboprophylaxis in patients undergoing elective total hip and knee Arthroplasy. Original article. 2013; 47(2):161-167.
12. NK Chandra *et al*. Incidence of DVT in Orthop patients undergoing MLLOG with or without thromboprophylaxis: A comparative study. JEMDS, 2015, 4(105).
13. Steven B Deitelzweig *et al*. Prev of VTE in orthop surg patient. Cleveland Clinic Journal of Medicine, 2008.
14. Jose Bosque *et al*. Relationship between deep vein thrombosis and pulmonary embolism following THA and TKA. 2012; 35(3):228-233.
15. Jawed Fareed, Cafer Adiquzzel *et al*. Differentiation of paretal anticoagulants n the prevension and treatment of venous thromboembolism. Thrombosis Journal, 2011.
16. Bharathi Kalyani. Low molecular weight heparin: Current evidence for its application in Orthopedic surgery. Current vascular pharmacology, 2010.
17. Nicolaas C Budhiparama, Matthew P Abdel *et al.* VTE prophylaxis for Hip and Knee Arthroplasty: Changing Trends. Curr Rev Musculoskeletal Med. 2014; 7(2):108-116.