

A Retrospective Observational Study to Compare the Efficacy of Fondaparinux with Enoxaparin in DVT Prophylaxis in Patients Undergoing Hemiarthroplasty

Anoop Sivasankara Pillai¹, Sangeetha Gopinath², Meenakshy Thriprayar Viswanathan²

¹Department of Orthopedics, SUT Academy of Medical Sciences, Thiruvananthapuram, Kerala, India,

²Department of Pharmacology, SUT Academy of Medical Sciences, Thiruvananthapuram, Kerala, India

ABSTRACT

Background: Major orthopedic surgery is a very important risk factor for deep vein thrombosis (DVT). Prophylactic agents for preventing DVT include unfractionated heparin, low-molecular-weight heparins, and fondaparinux. Use of low-molecular-weight heparins, however, is associated with an increased risk of bleeding. To date, there are few Indian studies comparing the efficacy of fondaparinux with enoxaparin. A comparison would be useful given the widespread use of fondaparinux in orthopedic patients. **Materials and Methods:** This retrospective observational study was undertaken in the orthopedic department of our hospital. All patients undergoing hemiarthroplasty between January 2016 and December 2017 were retrospectively analyzed using patient case files, hospital admission, and discharge database. Efficacy was assessed by the occurrence of a venous thromboembolic event, defined as DVT detected by ultrasonography, documented symptomatic DVT, or documented symptomatic pulmonary embolism. **Results:** Evaluation of case files of 71 patients who underwent hemiarthroplasty showed that fondaparinux (35) was as effective as enoxaparin (36). **Conclusions:** In patients who underwent major orthopedic surgery, enoxaparin was as effective as fondaparinux in preventing venous thromboembolism.

Key words: Efficacy, enoxaparin, fondaparinux, major orthopedic surgery

INTRODUCTION

The improvement in life expectancy has led to an increase in the incidence of hip fractures and hip replacement

surgeries in our country. Hip surgery is one of the major risk factors of deep vein thrombosis (DVT). However, in comparison to the Western population,^[1] the occurrence of DVT is surmised to be low in the Indian population.^[2] Hence DVT chemoprophylaxis is not routinely carried out in all patients undergoing major orthopaedic procedures.^[3,4] Some recent studies have shown that there is an increased occurrence of DVT in the Indian population, thereby justifying routine chemoprophylaxis.^[5-7]

A variety of thromboprophylactic regimens are available which include low-molecular-weight heparin (LMWH) and fondaparinux.

Fondaparinux acts by selectively inhibiting factor Xa, without any direct activity against factor IIa, while

Access this article online	
Website: www.mmj.net.in	Quick Response Code 
DOI: 10.15713/ins.mmj.44	

Address for correspondence:

Sangeetha Gopinath, Department of Pharmacology, SUT Academy of Medical Sciences, Thiruvananthapuram, Kerala, India. E-mail: sangeetha.twinkles@gmail.com

enoxaparin inhibits both factor IIa (thrombin) and factor Xa.^[8,9]

Many clinical trials have demonstrated that fondaparinux has superior efficacy.^[10-14] In contrast, a registry-based study, conducted in a large population of unselected patients, showed that fondaparinux was less effective than LMWH in preventing DVT.^[15]

This study was undertaken with the objective to compare their efficacy in actual clinical practice.

MATERIALS AND METHODS

The study was conducted in the orthopedic outpatient department of a tertiary care hospital. It was a retrospective observational study. The study was conducted according to the Declaration of Helsinki, and the study protocol was reviewed and approved by the Institutional Ethics Committee.

Patients

Patients of both sexes above 60 years of age who underwent elective hemiarthroplasty by the same surgeon were included in the study. Patients were excluded if they had a history of congenital or acquired bleeding disorder, had active bleeding, uncontrolled hypertension, liver, or renal impairment.

Study Design

All patients who underwent hemiarthroplasty, by the same surgeon between January 2016 and December 2017, were retrospectively analyzed using patient charts, hospital admission, and discharge database.

Patients who received post-operative thromboprophylaxis with either 2.5 mg s/c fondaparinux (Arixtra: Smithkline Beecham) or 60 mg enoxaparin (Clexane: Sanofi Aventis) were investigated in our study with regard to occurrence of venous thromboembolism (VTE) and death. Both were given as once daily S/c injections for 1 week starting from the 1st post-operative day morning. The usual protocol followed in our hospital is clinical evaluation at 2 weeks, 6 weeks, 3 months, 6 months, and again at 1 year. Routine ultrasonography evaluation is conducted at 2 weeks. Only symptomatic patients were evaluated with ultrasonography/computed tomography (CT) scans at later visits. Patients were followed up periodically for 1 year.

Outcome Measures

Patient charts were examined for report of any symptoms or signs of VTE or any other clinical event occurring during or after the completion of treatment. The occurrence of DVT assessed by Doppler ultrasound or fatal and non-fatal pulmonary embolism (PE) by CT was noted.

The primary efficacy outcomes was measured by the presence of a venous thromboembolic event, defined as DVT detected by ultrasonography, documented symptomatic DVT, or documented symptomatic PE.

Documented complications such as prolongation of the hospital stay and death were also noted.

Statistics

The two treatment groups were assessed for differences in baseline variables. Chi-square test was used to compare the data. All statistical analyses were carried out using the Statistical Package for the Social Sciences software IBM® Statistics Version 16.

RESULTS

Study Populations and Patient Characteristics

Between January 2016 and December 2017, 71 patients underwent hemiarthroplasty by the same surgeon. Of these, 35 patients (49.3%) received fondaparinux, 35 patients (50.7%) received enoxaparin.

Patients on either arms of the study were comparable in terms of age and sex [Table 1]. Similarly, specific surgical characteristics such as duration of surgery, need for transfusion, time to ambulation, and discharge were comparable between the two groups.

Incidence of VTE

One patient received enoxaparin developed leg swelling and was documented as having superficial

Table 1: Patient characteristic

Characteristic	Fondaparinux (n=35)	Enoxaparin (36)
Age (Mean)	71.74	71.8
Gender (M/F)	23 (66)/12 (34)	24 (67)/12 (33)

vein thrombosis. There was no occurrence of DVT among patients who received fondaparinux. This was not found to be statistically significant. There were no reports of fatal PE or DVT in both groups.

DISCUSSION

Our study demonstrates that the occurrence of venous thromboembolic events did not differ significantly between fondaparinux and enoxaparin. In the study by Bauer *et al.*, fondaparinux group had a significantly lower incidence of VTE (12.5%) than the enoxaparin group (27.8%) ($P = 0.06$).^[10]

A similar result was also demonstrated by Migita *et al.* in the Japanese population. Their study demonstrated that fondaparinux significantly reduced the incidence of DVT compared to enoxaparin.^[11]

Eriksson *et al.* study compared the efficacy of fondaparinux with enoxaparin in patients who underwent hip fracture surgery.^[12] In their study too, the incidence of VTE was significantly lower ($P < 0.001$) in the fondaparinux group (8.3%) than the enoxaparin group (19.1%). The incidence of symptomatic VTE, fatal and non-fatal PE was low, with no difference between the two groups.

The study by Lassen *et al.* demonstrated in elective hip replacement surgery reached the same conclusion demonstrating superior efficacy of fondaparinux ($P < 0.001$).^[13] The meta-analysis by Turpie also confirmed this finding.^[12]

In contrast to all these studies, a study done in unselected patients undergoing major orthopedic surgery demonstrated that fondaparinux was less effective in preventing DVT than LMWH.^[15]

Limitations

Our study was a retrospective observational study. The sample size was small.

CONCLUSIONS

Our study came to the conclusion that enoxaparin was as effective as fondaparinux in preventing VTE. This is at odds with most other studies evaluating these drugs. This has to be further evaluated by conducting studies in a large population of patients.

REFERENCES

1. Liberman JR, Hsu WK. Prevention of venous thromboembolic disease after total hip and knee arthroplasty. Current concepts review. *J Bone Joint Surg Am* 2005;87:2097-112.
2. Lee AD, Stephen E, Agarwal S, Premkumar P. Venous thrombo-embolism in India. *Eur J Vasc Endovasc Surg* 2009;37:482-5.
3. Mavalankar AP, Majmundar D, Sudha R. Routine chemoprophylaxis for DVT in Indian patients. *Indian J Orthop* 2007;41:188-93.
4. Jain V, Dhaon BK, Jaiswal A, Nigam V, Singla J. Deep vein thrombosis after total hip and knee arthroplasty in Indian patients. *Postgrad Med J* 2004;80:729-31.
5. Todi SK, Sinha S, Chakraborty A, Sarkar A, Gupta S, Das T, *et al.* Utilisation of deep venous thrombosis prophylaxis in medical/surgical intensive care units. *Indian J Crit Care Med* 2003;7:103-5.
6. Sen RK, Tripathy SK, Singh AK. Is routine thromboprophylaxis justified among Indian patients sustaining major orthopedic trauma? A systematic review. *Indian J Orthop* 2011;45:197-207.
7. Parakh R, Kakkar VV, Kakkar AK. Venous Thromboembolism (VTE) Core Group. Management of venous thromboembolism. *J Assoc Physician India* 2007;55:49-70.
8. Paolucci F, Claviés M, Donat F, Necciari J. Fondaparinux sodium mechanism of action: Identification of specific binding to purified and human plasma-derived proteins. *Clin Pharmacokinet* 2002;41:11-8.
9. Nutescu EA, Burnett A, Fanikos J, Spinler S, Wittkowsky A. Pharmacology of anticoagulants used in the treatment of venous thromboembolism *J Thromb Thrombolysis* 2016;41:15-31.
10. Bauer KA, Eriksson BI, Lassen MR, Turpie AG. Fondaparinux compared with enoxaparin for the prevention of venous thromboembolism after elective knee surgery. *N Engl J Med* 2001;344:1305-10.
11. Migita K, Bito S, Nakamura M, Miyata S, Saito M, Kakizaki H, *et al.* Venous thromboembolism after total joint arthroplasty: Results from a Japanese multicenter cohort study. *Arthritis Res Ther* 2014;16:R154.
12. Eriksson BI, Bauer KA, Lassen MR, Turpie AG. Fondaparinux compared with enoxaparin for the prevention of venous thromboembolism after hip-fracture surgery. *N Engl J Med* 2001;345:1298-304.
13. Lassen MR, Bauer KA, Eriksson BI, Turpie AG. Postoperative fondaparinux versus preoperative enoxaparin for prevention of venous thromboembolism in elective hip-replacement surgery: A randomised double-blind comparison. *Lancet* 2002;359:1715-20.
14. Turpie AG, Bauer KA, Eriksson BI, Lassen MR. Fondaparinux vs enoxaparin for the prevention of venous thromboembolism in major orthopedic surgery: A meta-analysis of 4 randomized double-blind studies. *Arch Intern Med* 2002;162:1833-40.

15. Donath L, Lützner J, Werth S, Kuhlisch E, Hartmann A, Günther KP, *et al.* Efficacy and safety of venous thromboembolism prophylaxis with fondaparinux or low molecular weight heparin in a large cohort of consecutive patients undergoing major orthopaedic surgery-findings from the ORTHO-TEP registry. *Br J Clin Pharmacol* 2012;74:947-58.

How to cite: Pillai AS, Gopinath S, Viswanathan MT. A Retrospective Observational study to compare the Efficacy of Fondaparinux with Enoxaparin in DVT prophylaxis in patients undergoing Hemiarthroplasty. *MIMER Med J* 2020;4(1):3-6.

Source of Support: Nil. **Conflicts of Interest:** None declared.

This work is licensed under a Creative Commons Attribution 4.0 International License. The images or other third party material in this article are included in the article's Creative Commons license, unless indicated otherwise in the credit line; if the material is not included under the Creative Commons license, users will need to obtain permission from the license holder to reproduce the material. To view a copy of this license, visit <http://creativecommons.org/licenses/by/4.0/> © Pillai AS, Gopinath S, Viswanathan MT. 2020