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

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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, the occurrence of DVT is surmised to be low in the Indian population. Hence DVT chemoprophylaxis is not routinely carried out in all patients undergoing major orthopaedic procedures. Some recent studies have shown that there is an increased occurrence of DVT in the Indian population, thereby justifying routine chemoprophylaxis.

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
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.\[13\]

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 thromboembolic event (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

| 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.[13]

**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.

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