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Efficacy and Safety of Apixaban and Enoxaparin for Thromboprophylaxis after Total Hip Arthroplasty

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Abstract: To explore its safety and efficacy for thromboprophylaxis of apixaban and enoxaparin after total hip arthroplasty (THA) patients. The study was designed as a prospective observational study, and all 70 patients who met the inclusion and exclusion criteria and underwent elective total hip (THA) arthroplasty between 1 January 2021 and 30 June 2022 were randomly assigned to Apixaban (Twice daily Dose 2.5 mg orally) or enoxaparin (Dose 60 mg every 24 hours subcutaneously), 35 patients were treated with apixaban and 35 patients were treated with enoxaparin. Apixaban treatment was started 12 to 24 hours after surgical wound closure and enoxaparin treatment was started 12 hours before surgery. A venogram was repeated at 42 days with postoperative prophylaxis. SPSS 28.0 was used to analyze the data, $P < 0.05$ was significant difference.The experiment compared the prices of them. The 70 patients included in the study were lost to follow-up due to possible reasons, and only 51 patients completed the trial in the end, including 26 patients apixaban and 25 patients enoxaparin. In studies apixaban at Dose 2.5 mg had similar to 60 mg daily and had similar bleeding characteristics. And there were no differences at 90-day. Price comparison prompts thatEnoxaparin cost more than apixaban throughout the trial period. symptomatic was lower in the apixaban group. Oral administration of apixaban showed better safety, similar efficacy, lower Price and better compliance hip arthroplasty in patients.

1. Introduction

Patients undergoing Total Hip Arthroplasty (THA) require effective thromboprophylaxis, as the incidence of embolism is as high as 40 to 60% [1].There were several options. Currently, low molecular heparin and sulphadoxine need to be injected subcutaneously; for prolonged use; and after hip surgery[2]. Enoxaparin and other low molecular weight heparins mainly inhibit factor Xa, but also inhibit thrombin to some extent; oral apixaban can effectively prevent thrombosis, and the oral way is easy to improve patient compliance [3-4].Clinical trials arthroplasty surgery have shown better or lower [5].Based on these studies, the present randomised prospective study: a trial of apixaban administered orally versus enoxaparin injection for anticoagulation to prevent venous thromboembolism was conducted to apixaban versus enoxaparin.

2. Methods

2.1 Study drug and assessment

The study design was a prospective observational study. The study included all patients who underwent elective total hip (THA) at our institution between 1 January 2021 and 30 June 2022.

2.2 Inclusion criteria

Patients were considered eligible if they underwent the relevant therapeutic measures taken in this randomised trial. All patients undergoing these procedures signed a written informed consent form.

2.3 Exclusion criteria

Known coagulation disorders; Active hepatobiliary disease; Hereditary (grade 1) or acquired bleeding or clotting disorders; Patients with preoperative detection of deep vein thrombosis and previous known/documented; Any condition for which surgery or anticoagulants are considered contraindicated by the investigator; Any condition for which surgery or anticoagulants are considered contraindicated by the investigator [6-7].

2.4 Price

The daily prices and total prices of Apixaban and Enoxaparin were compared during the trial period.

2.5 Therapeutic results

Symptomatic deep vein thrombosis, asymptomatic deep vein thrombosis, pulmonary embolism, and other efficacy results were collected.

2.6 Safety results

Bleeding incident; Wound-related complications; Systemic related complications.

Apixaban was started 12 to 24 hours and enoxaparin was started 12 hours before surgery. A venogram was repeated at 42 days with postoperative prophylaxis. Follow-up was performed during hospitalisation and 90 days after discharge to monitor all patients, and outcomes of other adverse events.

2.7 Data Analyses

SPSS 25.0 statistical software was used to analyze the data. The count data were expressed as rate (%). $P < 0.05$ was considered as the statistically significant difference.

3. Results

3.1 Patient

Between 1 January 2021 and 30 June 2022, total 70 patients with THA, including 35 patients were treated with apixaban and 35 patients were treated with enoxaparin, were eligible for this study. Due to possible reasons (inconvenient use of enoxaparin, higher price of enoxaparin, patients'

unwillingness to cooperate with late follow-up, and other factors) 9 patients were lost to apixaban, with a loss rate of 25.71%, and 10 patients were lost to enoxaparin, with a loss rate of 28.57%. The final statistical results showed that a total of 51 patients, including 26 patients treated with apixaban and 25 patients treated with enoxaparin, were eligible in this study. The patients aged 57.6 the apixaban and 60.3 years in the enoxaparin. There were 14 Men and 12 Women apixaban and 13 Men and 12 Women enoxaparin.

3.2 Therapeutic outcome (see Table 1 and Table 2)

Efficacy results were evident in 7 of the 51 patients. Three patients (11.54%) in the apixaban group suffered symptomatic DVT, while four patients (16.00%) suffered it. DVT in the enoxaparin group occurred before surgery and two during follow-up. Symptomatic DVT apixaban occurred before surgery in two cases and during hospitalisation after surgery in one case, with no abnormalities in the patients during follow-up. The risk of overall efficacy outcomes was not reduced using thromboprophylaxis.

3.3 Safety (Table 3)

There was one case of wound dehiscence in the enoxaparin group, no wound dehiscence in the apixaban group, (the site of intravenous injection: ecchymosis or petechiae). There was 1 case of leakage (bleeding from the surgical site).

Complications included: Among the neurological complications, transient ischaemic attack and psychosis occurred in 1 case 3.85% (1/26) in the apixaban group, and 1 case 4.0% (1/25) in the enoxaparin group; apixaban, urinary complications such as increased frequency or urinary incontinence occurred in 3.85% (1/26) of the patients, while enoxaparin (2/25) 8.0% of the patients developed urinary complications; pulmonary complications occurred in 4% (1/25) of patients in the enoxaparin group but not in the apixaban group; atrial fibrillation (AF) had to be switched to the therapeutic dose of enoxaparin, an upper respiratory tract infection (URTI); systemic anaphylactic reactions occurred in 1 patient in both the apixaban group and enoxaparin group; and systemic aches and pains was , and systemic tightening of the skin was in both the enoxaparin groups.

3.4 Price

Apixaban at 2.5 mg cost $7.07 RMB per day; enoxaparin at 60 mg each cost $47.6 RMB per day.Enoxaparin cost more than apixaban throughout the trial period.

Table 1: Comparison of the levels of D-dimer, coagulation and fibrinolytic indexes before and after treatment in the two groups ($\chi \pm s$)

Group	Time	D-dimer (mg/L)	Prothrombin time (s)	Fibrinogen (g/L)
Apixaban (n=26)	Preoperative	9.29±8.18	11±1.76	2.98±1.01
	1 day after surgery	5.18±3.22	11±1.12	3.11±0.98
	4 days after surgery	4.18±2.57	11±1.99	2.77±1.32
	7 days after surgery	4.18±2.19	12±1.78	2.26±1.48
	14 days after surgery	3.18±1.24	12±1.11	2.67±1.67
Enoxaparin (n=25)	Preoperative	10.29±6.17	12±1.37	2.77±1.14
	1 day after surgery	5.22±3.14	11±1.14	2.99±1.01
	4 days after surgery	4.11±2.18	11±1.57	2.87±1.24
	7 days after surgery	3.99±2.11	12±1.14	2.19±1.29
	14 days after surgery	2.88±2.01	12±1.39	2.48±1.48

Note: $P < 0.05$ for D-dimer; $P > 0.05$ for prothrombin time and fibrinogen when compared with the

same group before treatment.*P* values for D-dimer, prothrombin time and fibrinogen were greater than 0.05 in the apixa group and the baneoheparin group when compared between groups.

Table 2: Distribution of primary outcomes in the two group

	Asymptomatic deep vein thrombosis		SSymptomatic deep vein thrombosis		PPulmonary embolism		Death		Outcome	
	None (cases)	Occurrence (cases)	None (cases)	Ocurrence (cases)	None (cases)	Occurrence (cases)	None (cases)	Occurrence (cases)	None (cases)	Occurrence (cases)
Apixaban	26	0	23	3	26	0	26	0	23	3
Enoxaparin	25	0	21	4	25	0	25	0	21	4
P-value			0.533						0.533	

Table 3: Distribution of each secondary outcome in each group

	Therapeutic Drugs				
	Apixaban (case)		Enoxaparin (case)		
	None (cases)	Occurrence (cases)	None (cases)	Occurrence (cases)	*P*-value
Wound dehiscence	26	0	24	1	0.918
Clinically relevant non-major haemorrhage	25	1	22	3	0.869
Central Nervous System Abnormalities	25	1	24	1	0.912
Cardiovascular System Abnormalities	25	1	24	1	0.912
Upper Respiratory Tract Infection	26	0	24	1	0.918
Urinary tract abnormalities	25	1	23	2	0.989
Systemic allergic reactions	25	1	24	1	0.912
Other Systemic Abnormalities	25	1	24	1	0.912

4. Discussion

Efficacy outcomes: It was found that: the differences in the changes in D-dimer levels, coagulation and fibrinolytic indexes before and after drug administration were statistically significant, but the differences in the changes in D-dimer levels between them were not significant, and there was no statistically significant difference between the two for the changes in D-dimer levels, coagulation, and fibrinolytic indexes; during the period of treatment, symptomatic deep vein thrombosis was observed in 3 (11.54%) patients in the apixaban group, and symptomatic. When apixaban was compared with enoxaparin, the incidence of symptomatic DVT was lower in the apixaban group than in the enoxaparin group, but the difference was not statistically significant. Safety Outcomes: This is consistent with current guidelines for concomitant anticoagulation therapy.This is similar to Gómez-Outes A[8-10].This study was consistent with in substance and direct thrombin inhibitor (DTI) anticoagulant results were consistent[11-13].

Meanwhile, The results were similar to those of the American College of Chest Physicians for patients undergoing hip fracture surgery, where guidelines recommend the use of low molecular heparin, low-dose UFH, VKA, sulfadoxine, or aspirin[14-15]. Apixaban has a nonsignificant propensity for urinary complications and wound bleeding. This is similar to the results of a randomised double-blind trial studied by Lassen MR and other investigators: The results of this study were similar to those of Raskob GE and other investigators [16-17] .

This study also has some risk of serious complications, cardiovascular system complications such as atrial fibrillation and transient ischaemic attacks. This safety result has been seen in the studies of Gómez-Outes A, Lassen MR, Raskob GE and others. Similar safety outcomes to the present study were mentioned in the study by M R Lassen [18] .The study show that enoxaparin is more expensive than apixaban, which is similar to the findings of Antonio Gómez-Outes[19]: apixaban is a cost-saving in Spanish healthcare facilities.

5. Conclusion

In studies using apixaban in patients undergoing elective hip arthroplasty, apixaban at Dose 2.5 mg twice daily had similar efficacy at 60 mg daily and had similar bleeding characteristics. Extending this favourable balance of findings to patients undergoing elective hip arthroplasty: rivaroxaban at 2.5 mg twice daily was superior to enoxaparin at 60 mg daily, preventing one episode of major venous thromboembolism per 130 treated patients on a proportional basis without increasing the risk of bleeding.The present trial showed that apixaban administered orally has similar efficacy to enoxaparin, and that its main advantages for use in hip arthroplasty patients are a better safety profile, better cost-effectiveness and better compliance.

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