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COMPARISON IN TERMS OF SAFETY AND EFFICACY BETWEEN FONDAPARINUX AND ENOXAPARIN IN ACUTE CORONARY SYNDROME

Dr Vinod Kumar Consultant Physician, JK Health Services Jammu

Dr Ritu Bhagat* Senior Resident, Pathology GMC Jammu *Corresponding Author

Dr Shahbaz Khan Senior Resident, Medicine GMC Jammu

ABSTRACT

Introduction: Cardiovascular disease (CVD) became the most common cause of death worldwide. Today, it accounts for approximately 30% of deaths worldwide including 40% in high income countries and about 28% in low and middle income countries. Coronary artery disease (CAD) is typically defined as a more than 50% stenosis of any epicardial coronary artery.

Aim: A study to compare the efficacy and safety of fondaparinux with that of enoxaparin in patients of acute coronary syndrome.

Method and Materials: This is a cohort study of one year from Nov. 2014 to Dec. 2015 conducted in GMC Jammu. A total of 180 patients were included in the study. Of these, 90 patients were given fondaparinux and remaining 90 patients were given enoxaparin randomly.

Results: In the present study, there was no episode of major bleeding in both the study groups. The difference between the two groups was 1.11%, in terms of minor bleeding, which was not statistically significant.

Conclusion: We conclude that fondaparinux is as effective as enoxaparin in the early prevention of major outcomes in acute coronary syndrome. In addition, fondaparinux appears to be safe in terms of bleeding risk than enoxaparin, a benefit which may lead to long-term reduction in ischemic complications and death.

INTRODUCTION:

Acute coronary syndrome (ACS) refers to a constellation of clinical signs and symptoms produced by acute myocardial ischemia. It comprises unstable angina (UA), ST- segment elevation myocardial infarction (STEMI), and non-ST-segment elevation myocardial infarction (NSTEMI). The initial diagnosis of ACS is based on history, risk factors and to the associated electrocardiogram (ECG) findings. It was hypothesized that selective Xa inhibitors of coagulation factors located further upstream in the coagulation pathway might be safer with respect to bleeding by not inhibiting thrombin activity directly. Factor Xa has been identified as a potential target for the design of new anticoagulants as selective inhibitors. Xa would effectively block coagulation[1]. Fondaparinux sodium is the first in a new class of antithrombotic agents that selectively inhibit factor Xa. It is a small, totally synthetic molecule, developed based on the native pentasaccharide sequence (in heparin) that binds to antithrombin III and potentiates its antifactor Xa activity [2,3,4] . Fondaparinux binds specifically to antithrombin III and not to irrelevant plasma proteins [5], exhibits no inhibitory effect on platelet aggregation [6], and is unlikely to be associated with clinical heparin-induced thrombocytopenia, according to the results of studies conducted to date [6,7,8,9].

Method and Materials: this is a cohort study for a period of one year from Nov. 2014 to Dec. 2015 undertaken in Govt. Medical College, Jammu. All patients of acute coronary syndrome, who fulfilled the eligibility criteria, admitted in Cardiac Care Unit during the period of study were the subjects. After fully explaining the purpose of study and seeking written consent, the subjects were requested to participate in the study.

Inclusion criteria:

1. All patients aged above 18 years and below 75 years, irrespective of convenient risk factors like hypertension, diabetes mellitus, etc.
2. Both sexes are included
3. Patients diagnosed with unstable angina pectoris, ST-elevation MI, NSTEMI on the basis of history, physical examination, ECG changes and serum cardiac biomarkers.

Exclusion criteria :

1. Patients undergoing percutaneous coronary intervention (PCI).
2. Patients with active clinically significant bleeding, severe renal impairment (GFR < 30 ml/hr), presence of heparin-induced thrombocytopenia (HIIT)-type II, acute bacterial endocarditis, known hypersensitivity to fondaparinux or its excipients.
3. Patients weighing under 50 kg; patients with severe hepatic impairment.

Plan of ananlysis: At the end of the study, all the data thus obtained was put in a tabulated form and analysed using appropriate statistical technique and inferences were arrived at as per the aim and objectives of the study. Baseline characteristics in the two study groups were evaluated using chi-square test. A p-value of <0.05 was considered statistically significant.

Observation: This in-hospital study entitled "Comparison in terms of safety and efficacy between fondaparinux and enoxaparin in acute coronary syndrome" was Undertaken in Postgraduate Department of Medicine and Cardiac Care Unit of Government Medical College Hospital, Division of Cardiology, Jammu, during a period of 1 year w.e.f. November 2014 to December 2015. A total of 180 patients were included in the study. Of these, 90 Patients were included in the study. Of these, 90 patients were given fondaprinux and remaining 90 patients were given enoxaparin randomly.

Table 1: Sex distribution of patients included in fondapa rinux group and enoxaparin group

Sex	Fondaparinux group (n = 90) No. (%)	Enoxaparin group (n = 90) No. (%)	Total (n = 180) No. (%)
Male	63 (70.00)	62 (68.89)	125 (69.44)
Female	27(30.00)	28(31.11)	55 0.56)

Out of a total of 180 patients, 125 (69.44%) were males and 55 (30.56%) were females.

Table 2: Distribution of patients included in fondaparinux group and enoxaparin group according to history of smoking

H/o Smoking	Fondaparinux group		Enoxaparin group	
	Male (n = 63) No. (%)	Female (n = 27) No. (%)	Male (n = 62) No. (%)	Female (n = 28) No. (%)

Present	48 (76.20)	4 (14.81)	44 (70.97)	6(21.42)
Absent	15 (23.80)	23 (85.19)	18 (29.03)	22 (78.58)
Total	63	27	62	28

$X^2 = 0.31 p = 0.36$ (non-significant)

In fondaparinux group, 48 (76.20%) males were smokers and 15 (23.80%) were non-smokers, while 4 (14.81%) females were smokers and 23 (85.19%) were non-smokers. In enoxaparin group, 44 (70.97%) males were smokers and 18 (29.03%) were non-smokers, while 6 (21.42%) females were smokers and 22 (78.57%) were non-smokers.

Table 3: Distribution of patients included in fondaparinux group and enoxaparin group according to history of diabetes meilitus

	Fondaparinux group		Enoxaparin group	
H/o Diabetes meilitus	**Male (n = 63) No. (%)**	**Female (n = 27) No. (%)**	**Male (n = 62) No. (%)**	**Female (n = 28) No. (%)**
Present	30 (47.61)	9 (33.33)	26 (41.93)	11 (39.18)
Absent	33 (52.39)	18(66.67)	36 (58.07)	17(60.72)
Total	**63**	**27**	**62**	**28**

$X^2 = 0.76$ p=0.09 (non-significant)

In fondaparinux group, 30 (47.61%) males were diabetics and 33 (59.39%) were non-diabetics, while 9 (33.33%) females were diabetics and 18 (66.67%) were non-diabetics. In enoxaparin group, 26 (41.93%) males were diabetics and 36 (58.07%) were non- diabetics, while 11 (39.18%) females were diabetics and 17 (60.72%) were non-diabetics.

Table 4: Distribution of patients included in fondaparinux group and enoxaparin group according to history of hypertension

H/o Hypertension	**Fondaparinux group**		**Enoxaparin group**	
	Male (n = 63) No. (%)	**Female (n = 27) No. (%)**	**Male (n = 62) No. (%)**	**Female (n = 28) No. (%)**
Present	40 (63.50)	10 (37.03)	38 (61.30)	13 (46.42)
Absent	23 (36.50)	17 (62.97)	24 (38.70)	15(53.58)
Total	**63**	**27**	**62**	**28**

$x^2 = 0.02$ p=0.88 (non-significant)

In fondaparinux group, 40 (63.50%) males were hypertensive and 23 (36.50%) were normotensive, while 10 (37.03%) females were diabetics and 18 (66.67%) were non-diabetics. In enoxaparin group, 26 (41.93%) males were diabetics and 36 (58.07%) were non-diabetics, while 11 (39.18%) females were diabetics and 17 (60.72%) were non-diabetics.

Table 5: Distribution of patients included in fondaparinux group and enoxaparin group according to family history of ischaemic heart disease

	Fondaparinux group		**Enoxaparin group**	
Family H/o IHD	**Male (n = 63) No. (%)**	**Female (n = 27) No. (%)**	**Male (n = 62) No. (%)**	**Female (n = 28) No. (%)**
Present	3(4.76)	2 (7.40)	2 (3.20)	1 (3.57)
Absent	60 (95.24)	25 (92.60)	60 (96.80)	27 (96.43)
Total	63	27	62	28

p=0.72 (non-significant)

In fondaparinux group, 3 (4.76%) males had family history of IHD and 60 (95.24%) did not had family history of IHD, while 2 (7.40%) females had family history of IHD and 25 (92.60%) did not had family history of IHD. In enoxaparin group, 26 (41.93%) males were diabetics and 36 (58.07%) were non-diabetics, while 11 (39.18%) females were diabetics and 17 (60.72%) were non-diabetics.

Table 6: Depicting ECG findings in fondaparinux group and enoxaparin

Age group (in years)	**Fondaparinux group (n = 90)**		**Enoxaparin group (n = 90)**	
	Fresh ST changes	**No fresh ST changes**	**Fresh ST changes**	**No fresh ST changes**
18-27	—	1 (100.00)	—	1 (100.00)
28-37	—	8 (100.00)	—	8 (100.00)
38-47	2 (14.28)	12 (85.72)	1 (8.33)	11 (91.67)
48-57	1 (3.33)	29(96.67)	1 (3.03)	32 (96.67)
58-67	1 (3.57)	27(96.43)	3(13.04)	20 (86.96)
68-75	—	9 (100.00)	1 (7.69)	12 (97.31)
Total	4	86	6	84

In fondaparinux group, 4 (4.44%) patients show recurrent ischemia/myocardial infarction (as evidenced by fresh ST changes).

Table 7: Primary end points (at day 9) in fondaparinux group

Age group (in years)	**Hemorrhage No. (%)**	**Recurrent ischemia/MI No. (%)**	**Sudden death No. (%)**	**Recovery No. (%)**
18-27	—	—	—	1 (100.00)
28-37	—	—	—	8 (100.00)
38-47	—	2 (16.67)	—	12 (83.33)
48-57	—	1 (3.33)	—	29 (96.67)
58-67	1 (3.57)	1 (3.53)	—	26 (92.85)
68-75	—	—	—	9 (100.00)
Total	**1**	**4**	**—**	**85**

In the fondaparinux group, 4 (4.44%) patients had recurrent ischemia/MI, 1 (1.11%) patient had hemorrhage (major/minor) and 85 patients showed recovery without any recurrent ischemia/MI/death/hemorrhage.

Table 8: Primary end points (at day 9) in enoxaparin group

Age group (in years)	**Hemorrhage No. (%)**	**Recurrent ischemia/MI No. (%)**	**Sudden death No. (%)**	**Recovery No. (%)**
18-27	—	—		1 (100.00)
28-37	—	—	—	8 (100.00)
38-47	—	1 (8.33)	—	11 (96.67)
48-57	—	1 (3.03)	—	32 (96.67)
58-67	1 (4.35)	3 (13.04)	—	19 (82.60)
68-75	1 (7.69)	1 (7.69)	—	11 (84.61)
Total	**2**	**6**	**—**	**82**

In the fondaparinux group, 4 (4.44%) patients had recurrent ischemia/MI, 1 (1.11%) patient had hemorrhage (major/minor) and 85 patients showed recovery without any recurrent ischemia/MI/death/hemorrhage.

Table 9: Comparison between fondaparinux group and enoxaparin group in terms of primary end points

Fisher's Exact test p = 1.00 (non-significant) for hemorrhage

$X^2 \sim 0.42 p = 0.51$ (non-significant) for recurrent ischemia/MI.

Primary end points	**Fondaparinux group (n = 90) ~ No. (%)**	**Enoxaparin group (n = 90) No. (%)**
Hemorrhage	1 (1.11)	2 (2.22)
Recurrent ischemia/MI	4 (4.44)	6 (6.66)
Sudden death		—
Recovery	85 (94.44)	82 (91.11)
Total	**90**	**90**

DISCUSSION:

This in-hospital study entitled "Comparison in terms of safety and efficacy between fondaparinux and enoxaparin in acute coronary syndrome" was undertaken in the Post Graduate Department of Medicine and Cardiac Care Unit of Government Medical College Hospital, Division of Cardiology, Jammu during a period of 1 year w.e.f. November 2014 to December 2015. A total of 180 patients were included in this study.

In the present study, out of 180 patients, 125 (69.44%) were males and 55 (30.56%) were females. In our study, 90 patients each were in the fondaparinux and enoxaparin group. In this study, there was 63 (70%) males and 27 (30%) females in the fondaparinux group, whereas there are 62 (68.89%) males and 28 (31.11 %) females in the enoxaparin group.

In the study by Budaj et al. (2006)[10], there was 62% males and 38% femaies which is almost similar to our study. In our study, the mean age was 53.9 ± 11.35 years in the fondaparinux group and it was 53.65 ± 12.76 years in the enoxaparin group. In the study by Yusuf et al. (2006)[11], mean age was 66.6 ± 10.8 years in fondaparinux group, and was 66.6 ±11.0 years in the enoxaparin group.

In our study, there were 63.5% hypertensive males in the fondaparinux group and 61.3% hypertensive males in enoxaparin group. In the study by Budaj et al. (2006)[10], there were 66.9% hypertensive males, which is almost similar to that of our study. In our study, 43.33% patients were having diabetes in fondaparinux group and 41.11 % were having diabetes in the enoxaparin group. In the study by Yusuf ef al. (2006)[11], 25.3% patients were having diabetes in the fondaparinux group, and 25% were having diabetes in the enoxaparin group.

In our study, 55.55% patients were having hypertension in the fondaparinux group, whereas 56.67% patients were having hypertension in the enoxaparin group. In the study by Yusuf ef al. (2006)[11], there were 67.4% and 67% patients in the fondaparinux and enoxaparin group, respectively.

In our study, there were 57.78% and 55.56% smokers in the fondaparinux and enoxaparin group, respectively. In the study by Yusuf ef al. (2006)[11], there were 54.1% and 54.6% smokers in the fondaparinux and enoxaparin group, respectively. In the present study, ST depression >1 mm was present in 54.44% patients in both fondaparinux and enoxaparin group, respectively. In the study by Yusuf ef al. (2006)[11], ST depression >1 mm was present in 51.7% patients and 50.3% patients in fondaparinux and enoxaparin group, respectively. In the present study, 4.44% patients (n = 4) in the fondaparinux group and 6.67% (n =6) patients in the enoxaparin group showed the occurrence of recurrent ischemia/Ml as evidenced by ECG changes and troponin levels at day 9.

In the study by Yusuf et al. (2006)[11], the number of patients with primary outcome events (recurrent ischemia/Ml and death was similar in two groups (579 with fondaparinux (5.8%) versus 573 with enoxaparin 5.7%). In the present study,1 patient (1.11%) in the fondaparinux group and 2 patients (2.22%) in the enoxaparin group developed hemorrhagic complications. In the study by Mehta et al. (2008)[12], fondaparinux reduced major bleeding by 41% (3.4% in control group versus 2.1% in the fondaparinux group). In the study by Yusuf et al. (2006)[11], the 2.2% patients (n = 217) in the fondaparinux group and 4.1% patients (n = 412) in the enoxaparin group developed hemorrhagic complications showing a reduction of 48%.

CONCLUSION :

Thus , from the observations of the present study,we conclude that fondaparinux is as effective as enoxaparin in the early prevention of major outcomes in acute coronary syndrome. In addition, fondaparinux appears to be safe in terms of bleeding risk than enoxaparin, a benefit which may lead to long-term reduction in ischemic complications and death.

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